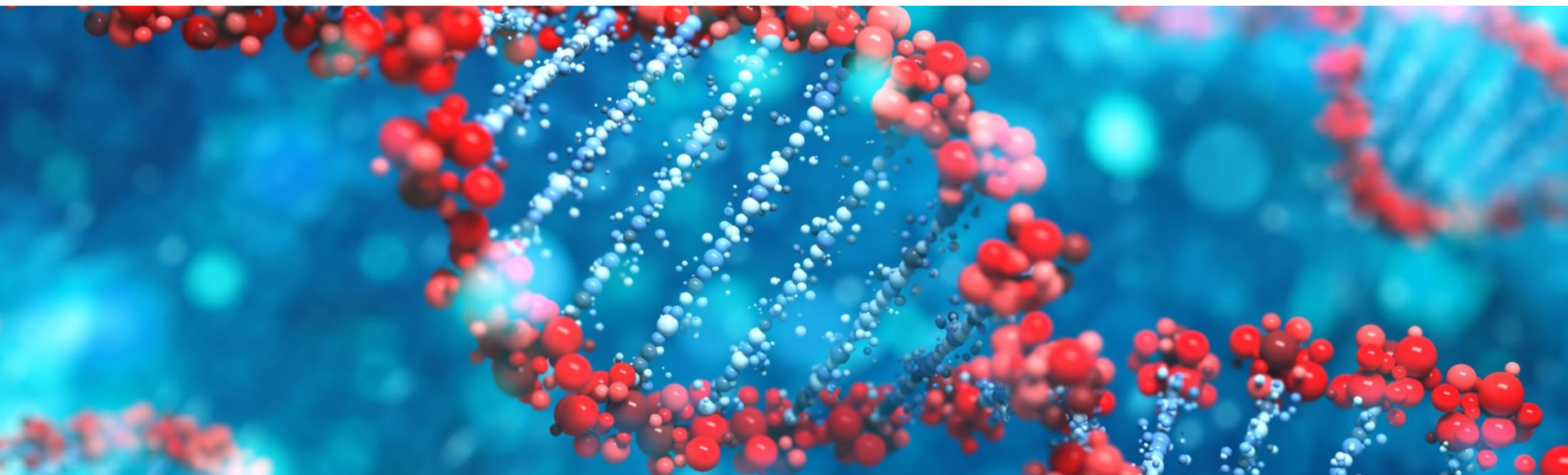


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# Turning innovation into patients benefit

*Karl Mahler, Head Investor Relations*

*Zuerich, August 2016*



This presentation contains certain forward-looking statements. These forward-looking statements may be identified by words such as ‘believes’, ‘expects’, ‘anticipates’, ‘projects’, ‘intends’, ‘should’, ‘seeks’, ‘estimates’, ‘future’ or similar expressions or by discussion of, among other things, strategy, goals, plans or intentions. Various factors may cause actual results to differ materially in the future from those reflected in forward-looking statements contained in this presentation, among others:

- 1 pricing and product initiatives of competitors;
- 2 legislative and regulatory developments and economic conditions;
- 3 delay or inability in obtaining regulatory approvals or bringing products to market;
- 4 fluctuations in currency exchange rates and general financial market conditions;
- 5 uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products;
- 6 increased government pricing pressures;
- 7 interruptions in production;
- 8 loss of or inability to obtain adequate protection for intellectual property rights;
- 9 litigation;
- 10 loss of key executives or other employees; and
- 11 adverse publicity and news coverage.

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## **Performance update**

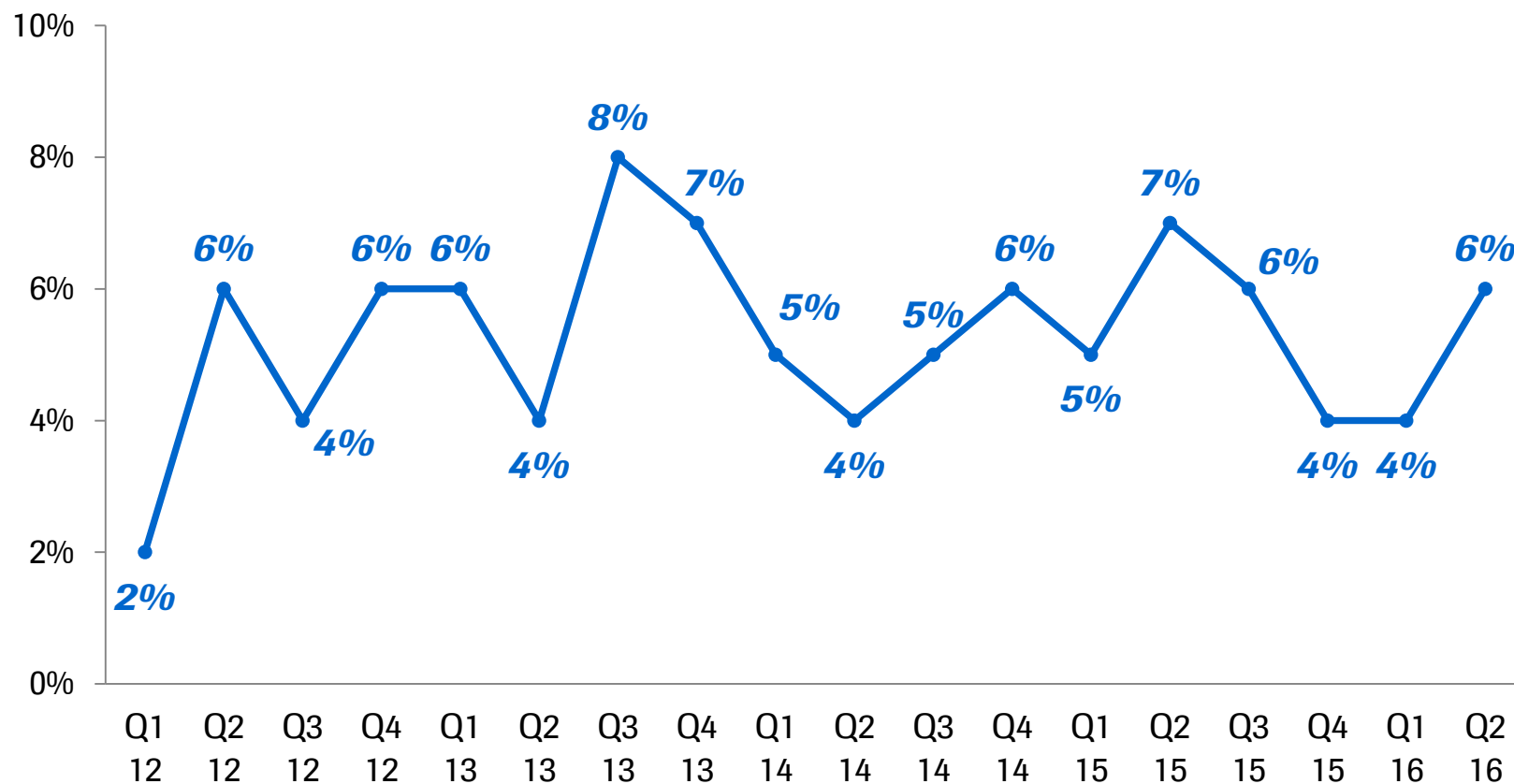
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**Innovation and differentiation**

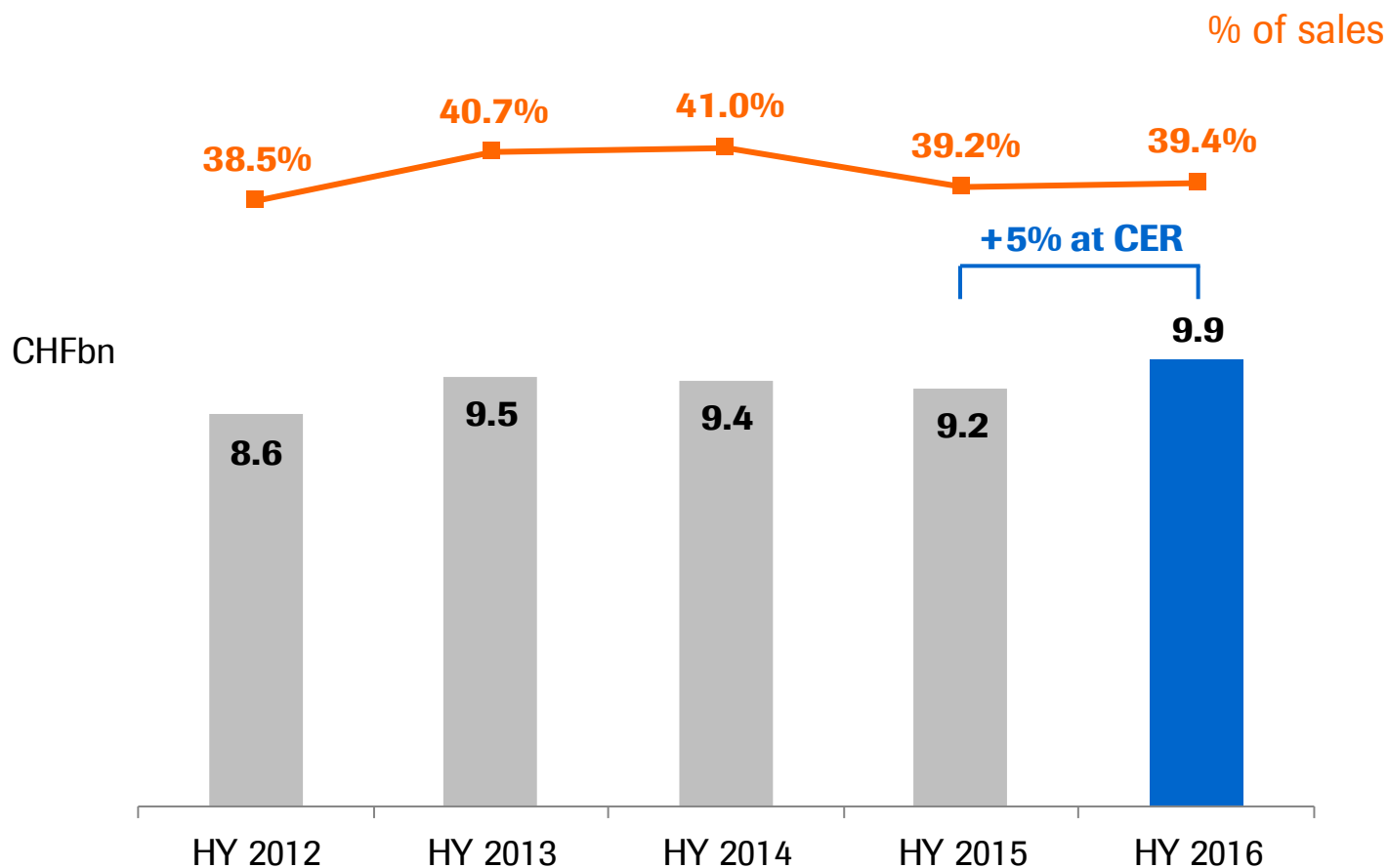
**Improving the standard of care**

**Outlook**

# Q2 2016: Sales growth for fifth consecutive year



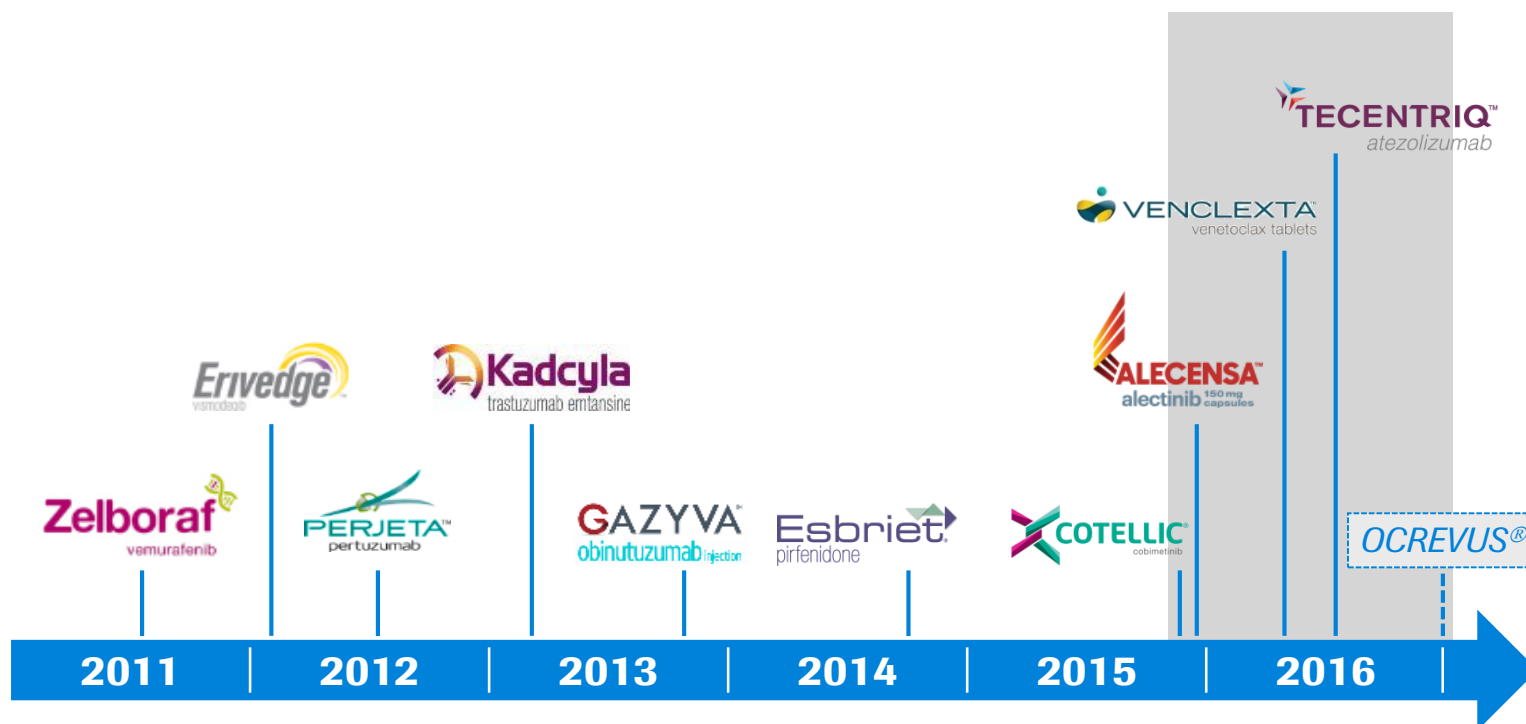
# HY 2016: Strong core operating profit & margin



# Continued leadership in innovation

## *Launches at historical high*

5 NME launches in a year



**Performance update**

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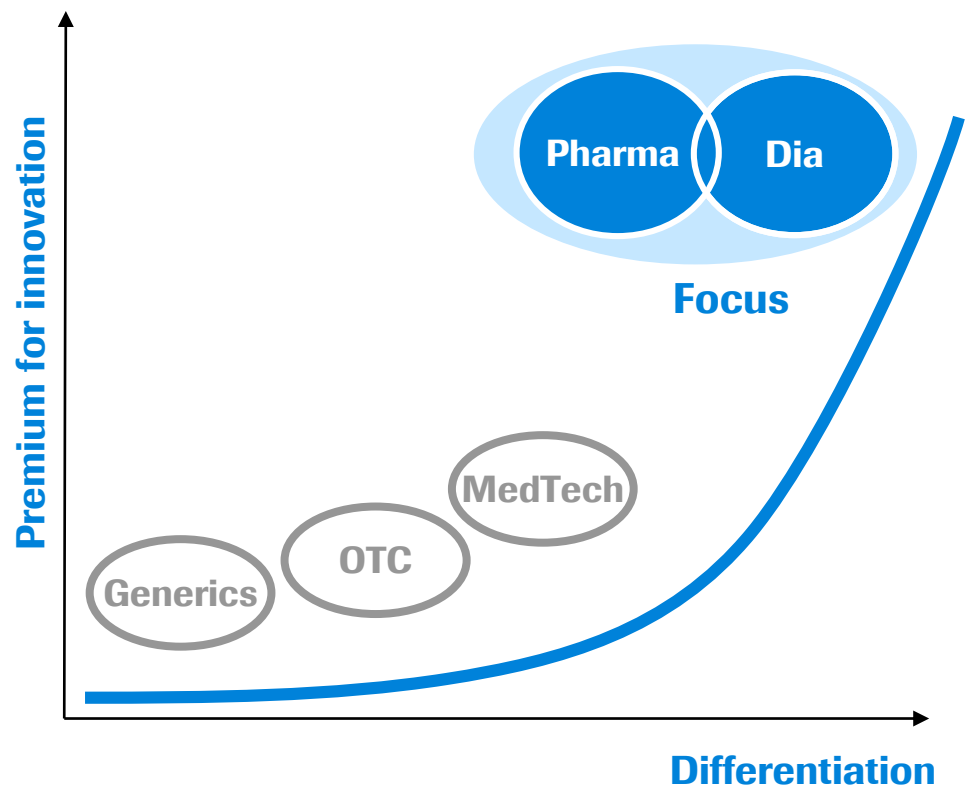
**Innovation and differentiation**

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**Improving the standard of care**

**Outlook**

# Roche strategy: Focused on medically differentiated therapies



## Regulators:

Optimised benefit / risk ratio

## Payors:

Optimised benefit / cost ratio



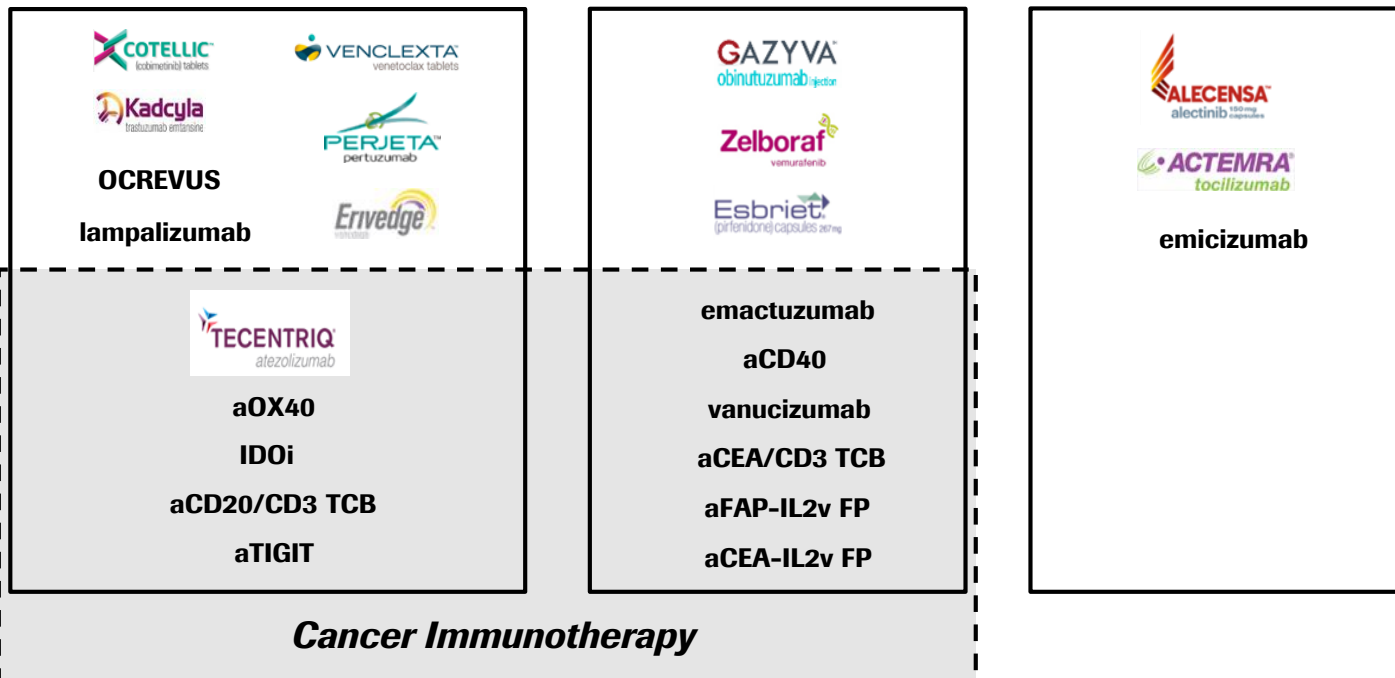
# Pillars of early R&D

## *Preserving cultures – increasing collaboration in CIT*

**Genentech**  
A Member of the Roche Group

**Roche**

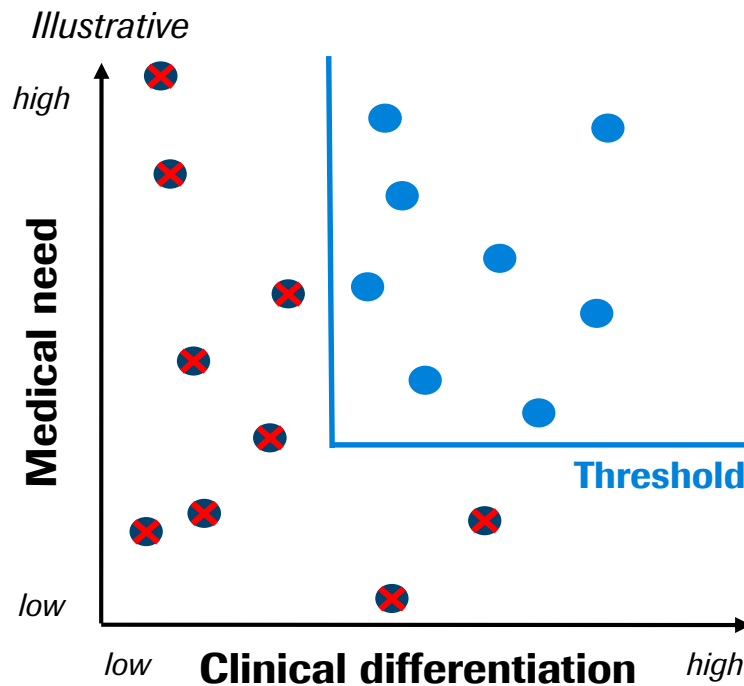
**CHUGAI**



# Approach towards innovation

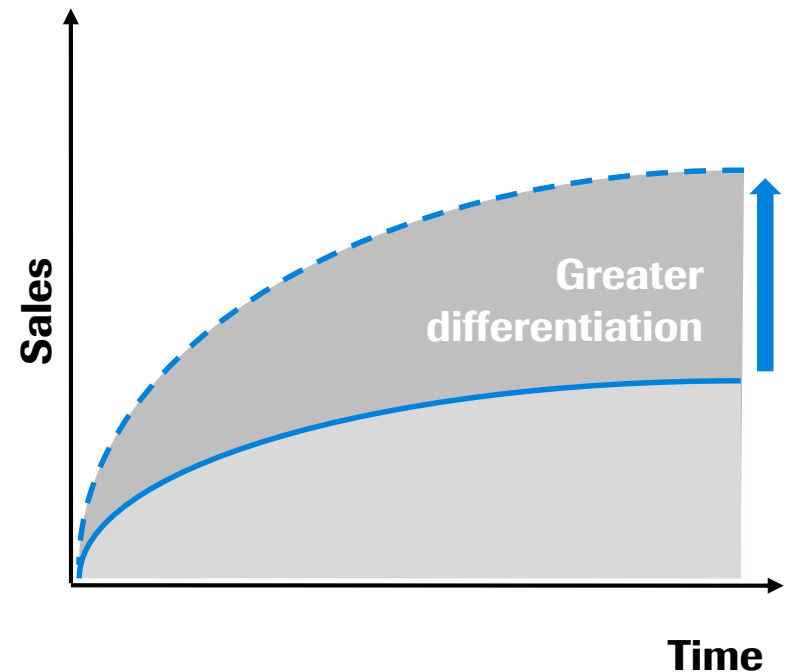
## *Prioritizing rigorously*

**We select at late stage entry**



- Continued
- ✕ Disqualified

**...to increase sales potential**



**Performance update**

**Innovation and differentiation**

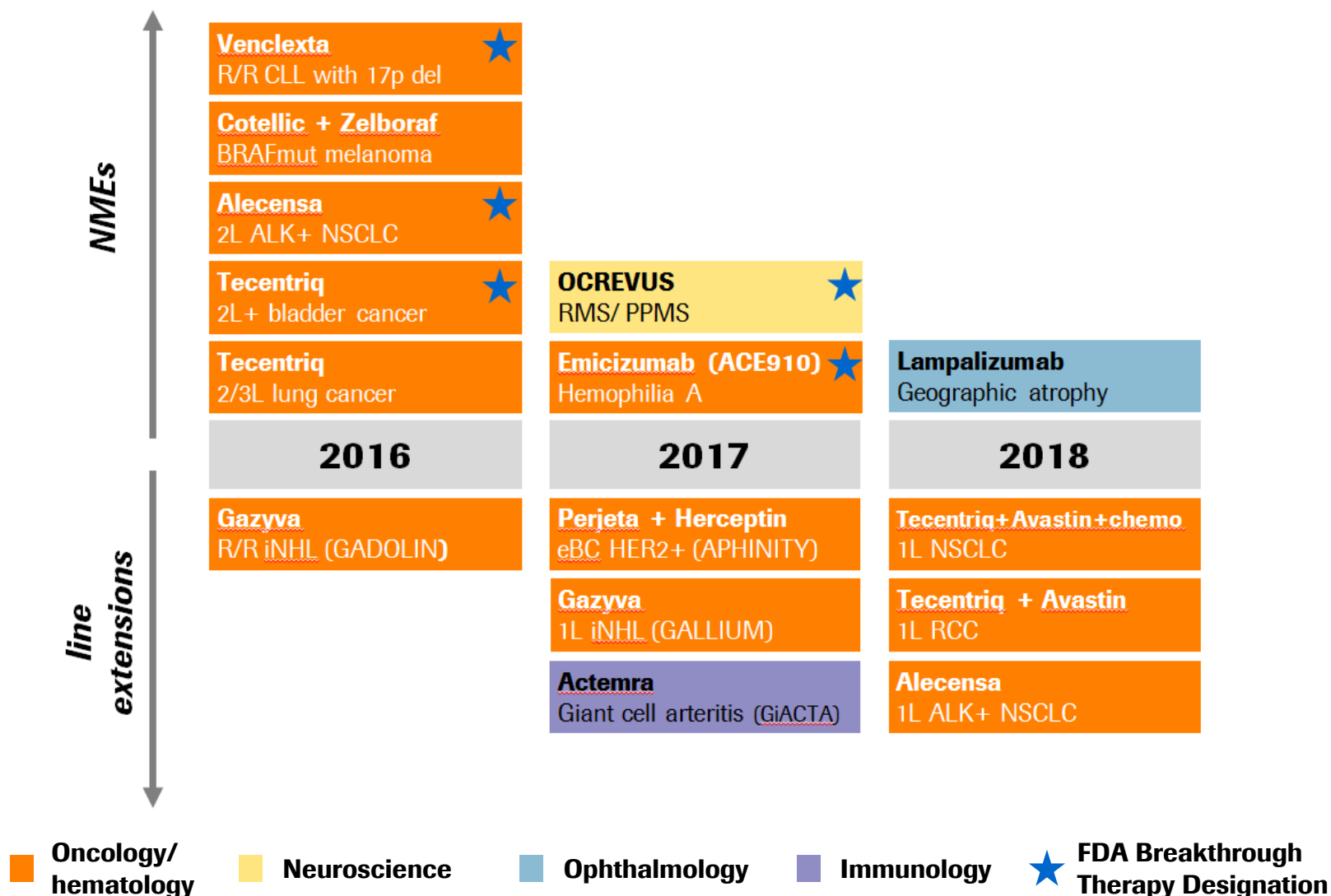
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**Improving the standard of care**

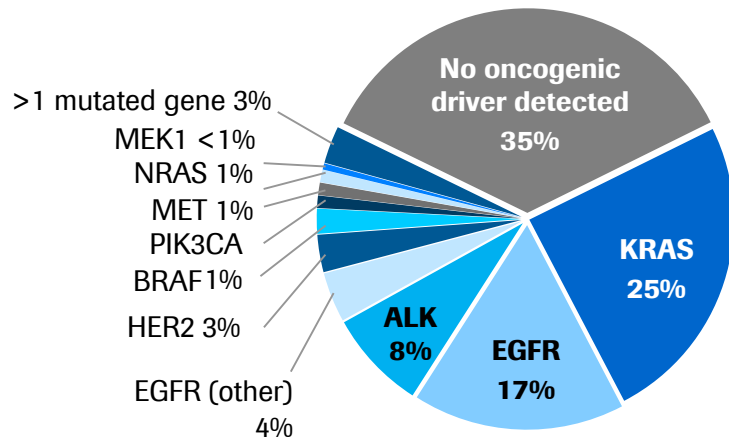
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**Outlook**

# 2016 onwards: Significant launch activities



# Why cancer immunotherapy is transformative



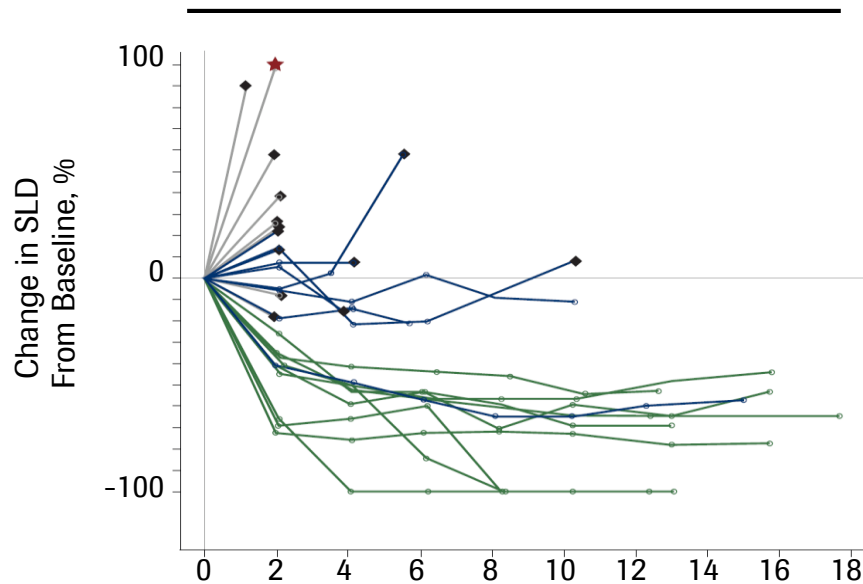
*“In the last two decades we've focused on hundreds of oncogenes as drivers in cancer, each one defining a different disease and a different treatment....*

*The immune system sees cancer as one disease. Now we can turn our focus to enhancing the immune system's ability to see the tumour.”*

*Gordon Freeman, Ph.D.  
Dana Farber Cancer Institute  
At CITC Advisory Board, Jan 21, 2016*

# Significant variability in treatment response to cancer immunotherapy

## Ph1 Tecentriq monotherapy UBC: IC2/3

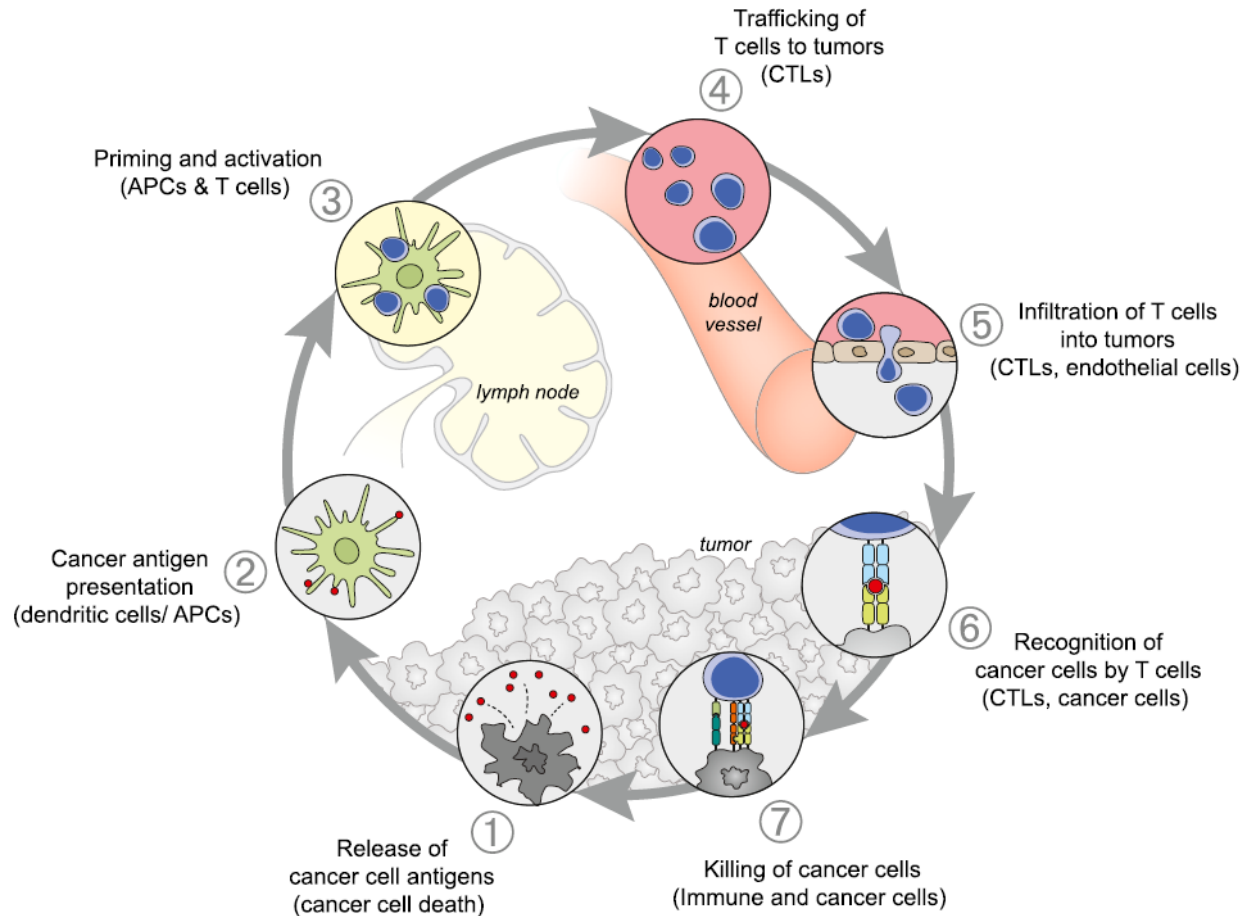


**PROGRESSIVE DISEASE (PD)**

**STABLE DISEASE (SD)**

**DURABLE RESPONSES (PR/CR)**

# The 7 steps of the cancer immunity cycle guide our prioritization framework for development



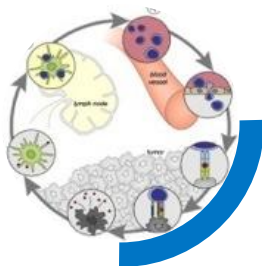
# Different tumours show different immune phenotypes and will need different solutions

## Inflamed

Melanoma

Lung

Bladder



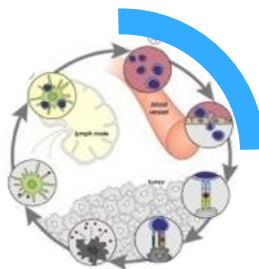
CD8+ T cells infiltrated,  
but non-functional

Accelerate or remove brakes  
on T-cell response

## Immune Excluded

TNBC

Colorectal



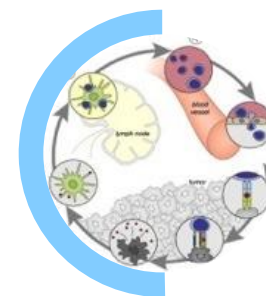
CD8+ T cells accumulated but  
not efficiently infiltrated

Bring T-cells in contact  
with cancer cells

## Immune Desert

Gastric

Ovarian



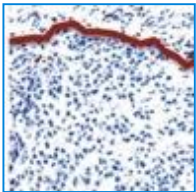
CD8+ T cells absent  
from tumor and periphery

Increase number of  
antigen-specific T-cells or  
increase antigen presentation



# Immune phenotypes and the cancer immunity cycle

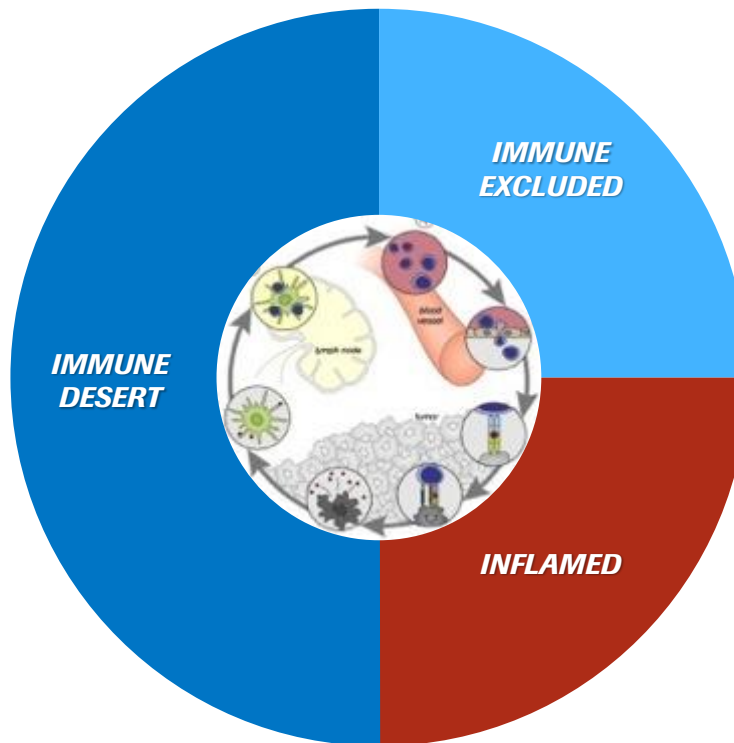
## IMMUNE DESERT



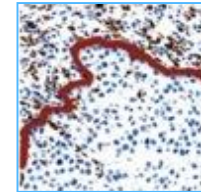
**CD8+ T cells are absent from tumor and its periphery**

### Key Questions:

- Main barriers?
- Optimally driving both antigen presentation and T cell activation



## IMMUNE EXCLUDED

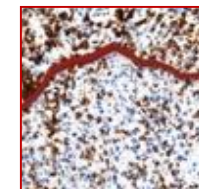


**CD8+ T cells accumulated but have not efficiently infiltrated**

### Key questions:

- optimally support trafficking of T cells into tumors

## INFLAMED

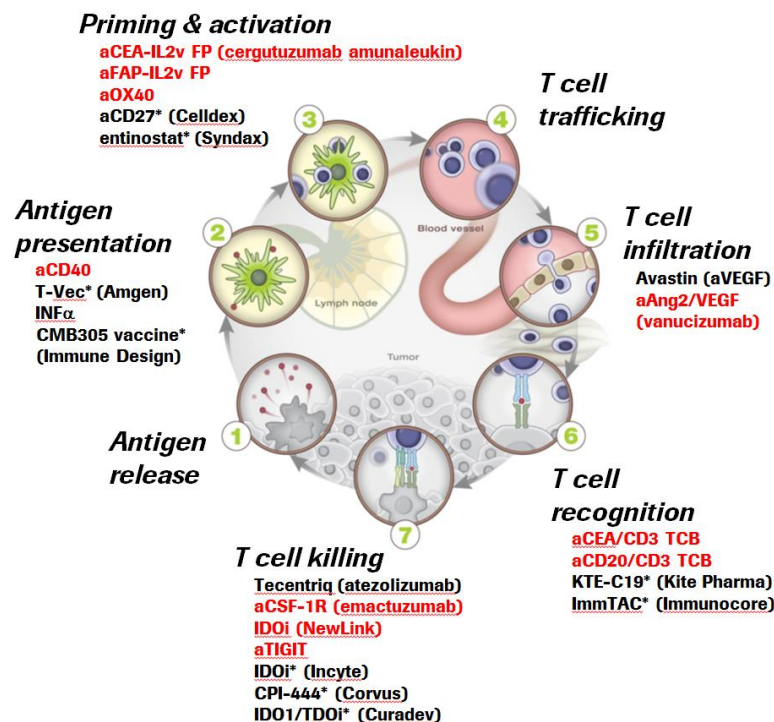


**CD8+ T cells infiltrated, but are non-functional**

### Key questions:

- enhance T cell function, role of tumor micro-environment

# A rich pipeline: 9 NMEs and a minimum of 10 combinations reading out within 2 years



	Compound 1	Compound 2	Phase	Readout**
2	aCD40	+ Tecentriq	Ph I (n=110)	2017
	aCD40	+ vanucizumab	Ph I (n=170)	2017
	aCD40	+ emactuzumab	Ph I (n=120)	2017
3	aCEA-IL2v FP	+ Tecentriq	Ph I (n=75)	2017
	aFAP-IL2v FP		Ph I (n=60)	2017
	aOX40		Ph I (n=400)	2017
	aOX40	+ Tecentriq	Ph I (n=360)	2017
5	vanucizumab		Ph II McCave (n=190)	2016
	vanucizumab	+ Tecentriq	Ph I (n=40)	2017
6	aCEA/CD3 TCB		Ph I (n=100)	2017
	aCEA/CD3 TCB	+ Tecentriq	Ph I (n=100)	2017
	aCD20/CD3 TCB		Ph I (n=170)	2017
7	emactuzumab	+ Tecentriq	Ph I (n=162)	2017
	IDOi	+ Tecentriq	Ph I (n=224)	2017
	aTIGIT	+ Tecentriq	Ph I (n=300)	2017

■ Clinical data within 2 years

Chen and Mellman. Immunity 2013;

\* CIT NMEs from partners in external collaborations; \*\* Outcome studies are event driven, timelines may change; NME=new molecular entity; CIT=cancer immunotherapy; FP=fusion protein; TCB=T-cell bispecific;

# A rich pipeline: Program by tumour type

## Solid tumors

### Solid tumors

Tecentrig		Ph1
Tecentrig	±chemo ±Avastin	Ph1
Tecentrig	+Cotellic	Ph1
aOX40	±Tecentrig	Ph1
aCEA/CD3 TCB	±Tecentrig	Ph1
IDOi	±Tecentrig	Ph1
emactuzumab	±Tecentrig	Ph1
aCEA-IL2v FP	±Tecentrig	Ph1
aFAP-IL2v FP		Ph1
aCD40	±Tecentrig	Ph1
emactuzumab	±aCD40	Ph1
aCD40	+vanucizumab	Ph1
Tecentrig	+vanucizumab	Ph1
aTIGIT	±Tecentrig	Ph1
Tecentrig	+daratumumab*	Ph1
Tecentrig	+IFN or ipilimumab*	Ph1
Tecentrig	+A2Ai*	Ph1
Tecentrig	+varilumab*	Ph1

### Bladder

Tecentrig (2L+ UBC)	✓
Tecentrig +BCG (NMIBC)	Ph1
Tecentrig (2L+ UBC)	<b>Ph3</b>
Tecentrig (Dx+ adjuvant MIBC)	<b>Ph3</b>
Tecentrig + chemo (1L mUC)	<b>Ph3</b>

### Lung (NSCLC & SCLC)

Tecentrig (2L/3L)	Ph2 filed/ <b>Ph3</b>
Tecentrig (1L Dx+)	<b>Ph3</b>
Tecentrig +chemo (3x 1L trials)	<b>Ph3</b>
Tecentrig +chemo ±Avastin (1L)	<b>Ph3</b>
Tecentrig (adjuvant)	<b>Ph3</b>
Tecentrig +Tarceva or Alecensa	Ph1
Tecentrig +chemo (SCLC)	<b>Ph3</b>
Tecentrig +epacadostat*	Ph1

### Melanoma

Tecentrig +Zelboraf ±Cotellic	Ph1
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### Ovarian

Tecentrig +rucaparib*	Ph1
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## Hematological tumors

Tecentrig	±lenalidomide	±daratumumab*	(R/R MM)	Ph1
Tecentrig	±azacitidine		(MDS)	Ph1
Tecentrig	+Gazyva or +tazemetostat*		(R/R FL and DLBCL)	Ph1
Tecentrig	+Gazyva	+polatuzumab	(R/R FL and DLBCL)	Ph2
Tecentrig	+Gazyva	+lenalidomide	(R/R FL and DLBCL)	Ph1
Tecentrig	+Gazyva	+bendamustin or CHOP	(1L FL and DLBCL)	Ph1
aCD20/CD3 TCB				Ph1
Tecentrig	+CD19 CAR-T*		(refractory aNHL)	Ph1

### Breast (TNBC & HER2+)

Tecentrig	+chemo (TNBC)	<b>Ph3</b>
Tecentrig	+Kadcyla or Herceptin+ Perjeta (HER2+)	Ph1
Tecentrig	+T-VEC*	Ph1
Tecentrig	+entinostat*	Ph2

### RCC

Tecentrig	±Avastin	Ph2
Tecentrig	+Avastin	<b>Ph3</b>

### Sarcoma

Tecentrig	+CMB305 (NY-ESO-1)*	Ph2
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### Colon

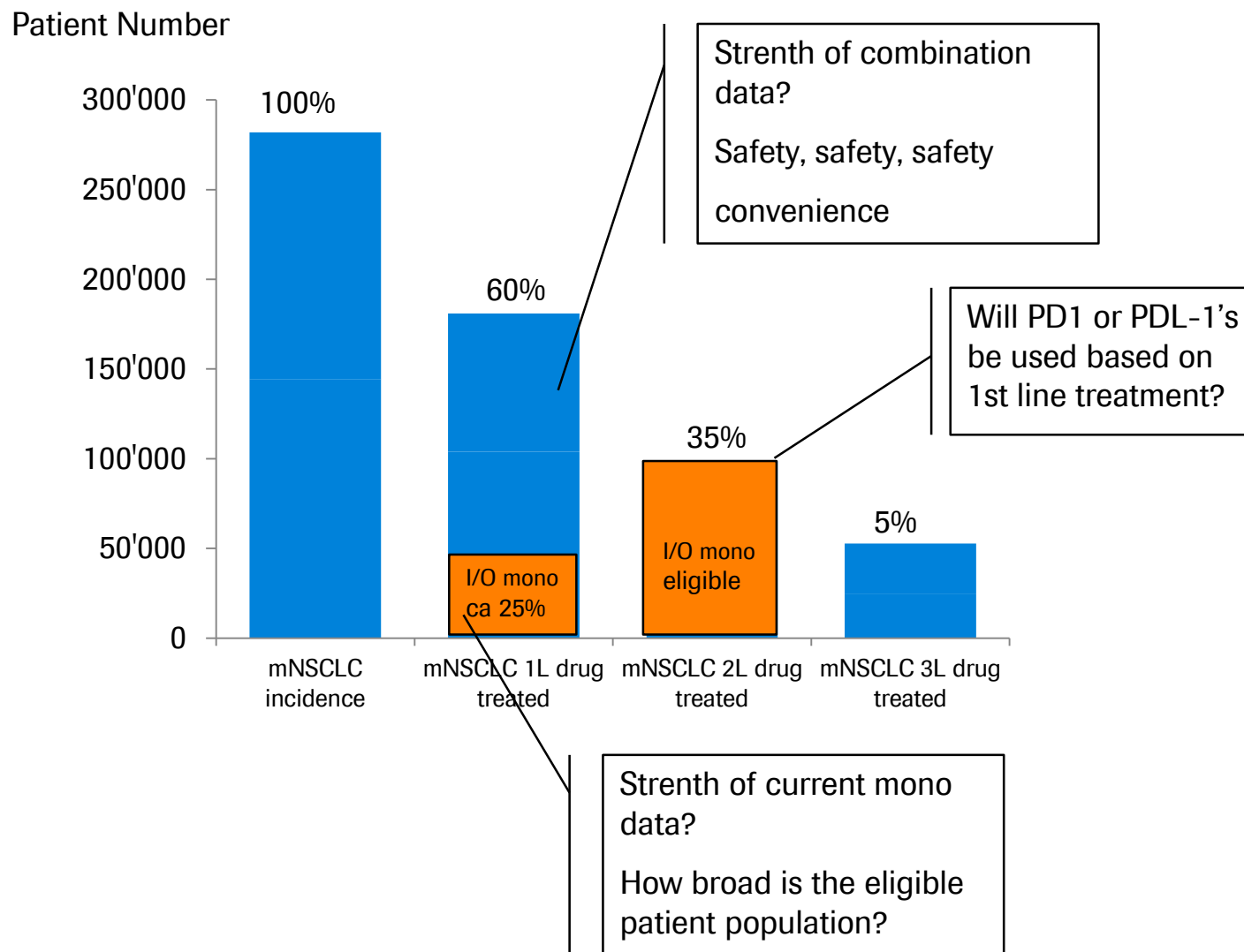
Tecentrig	+Cotellic (3L+)	<b>Ph3</b>
Tecentrig	+T-VEC*	Ph1

✓ = approved; \*External collaborations; Other CIT NMEs besides Tecentrig

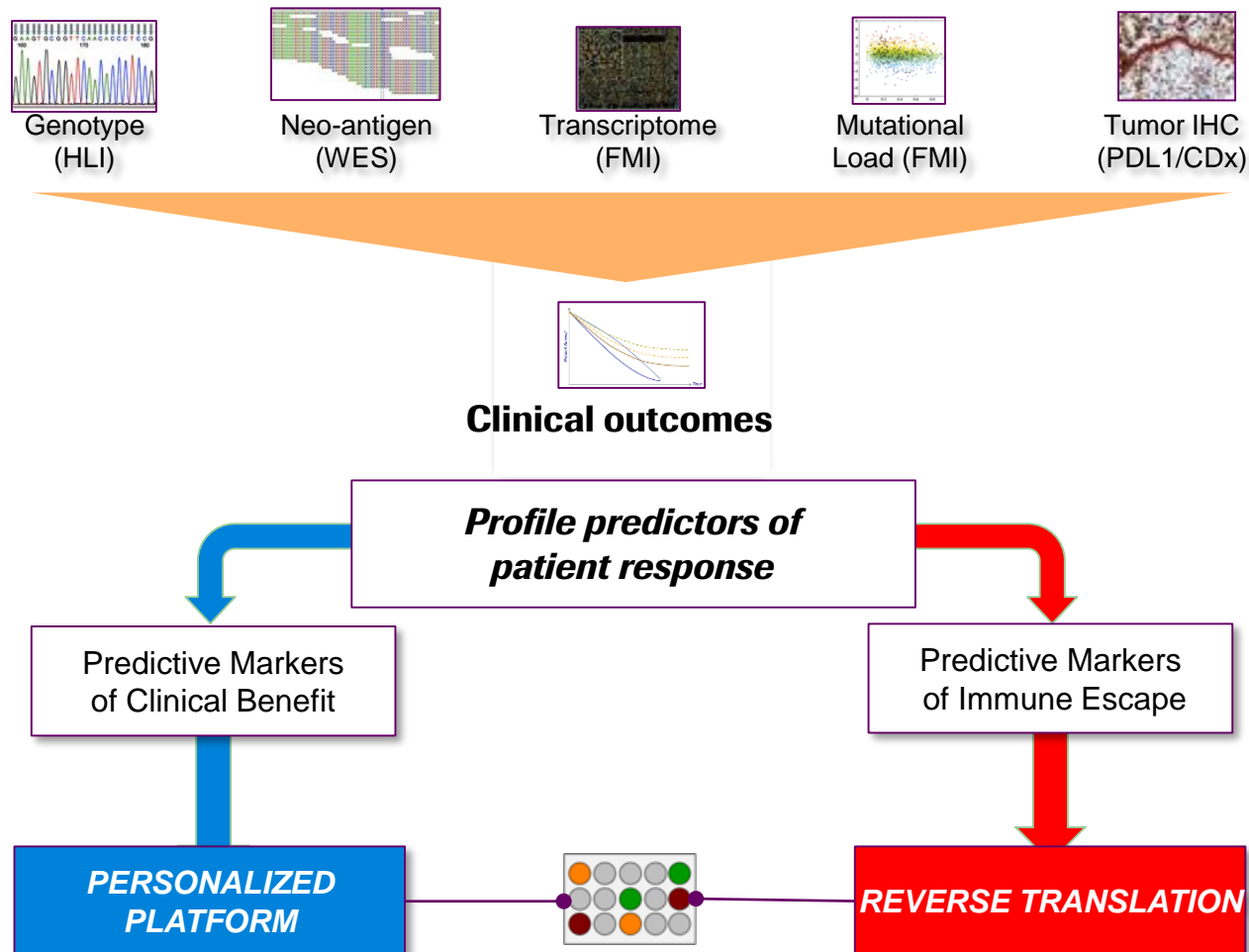
As of July 21, 2016

# mNSCL: Treatment algorithm

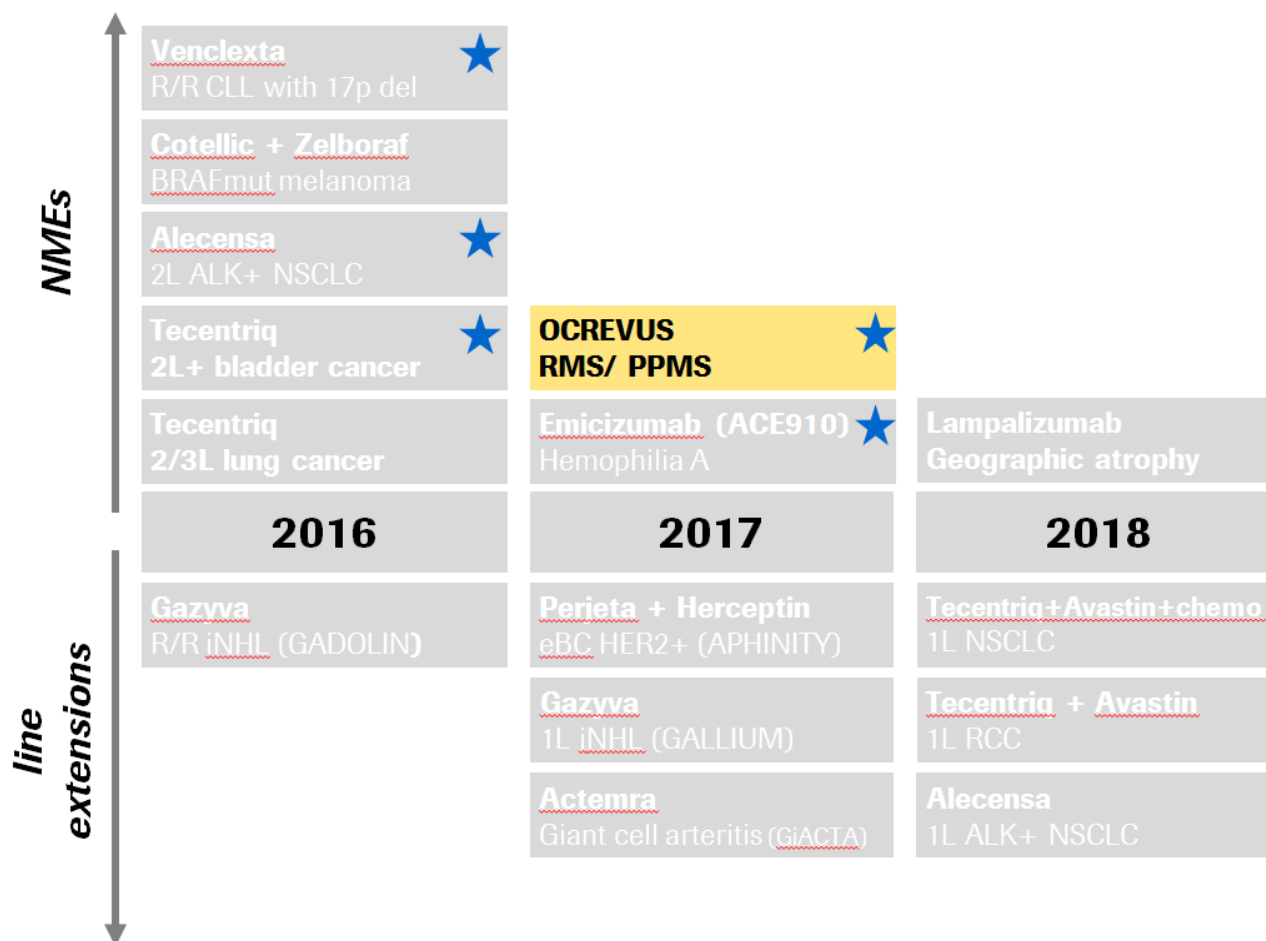
*Efficacy but also safety will play a major role*



# Identify and utilize relevant biomarkers to deliver personalized medicine

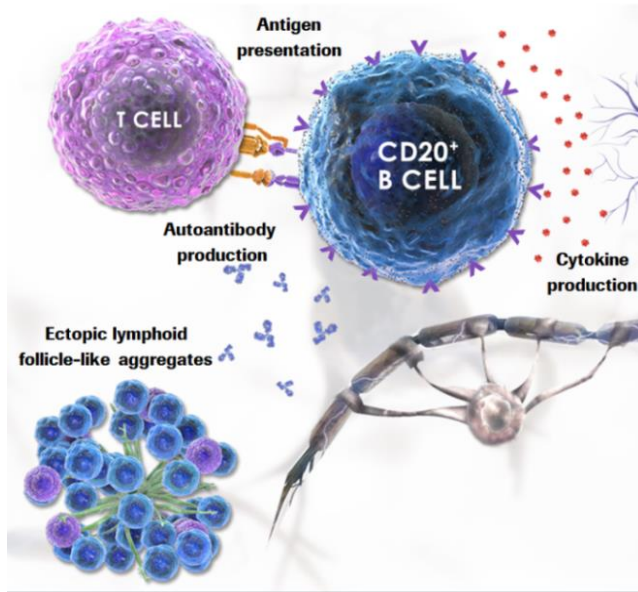


# OCREVUS: First medicine active in RMS and PPMS



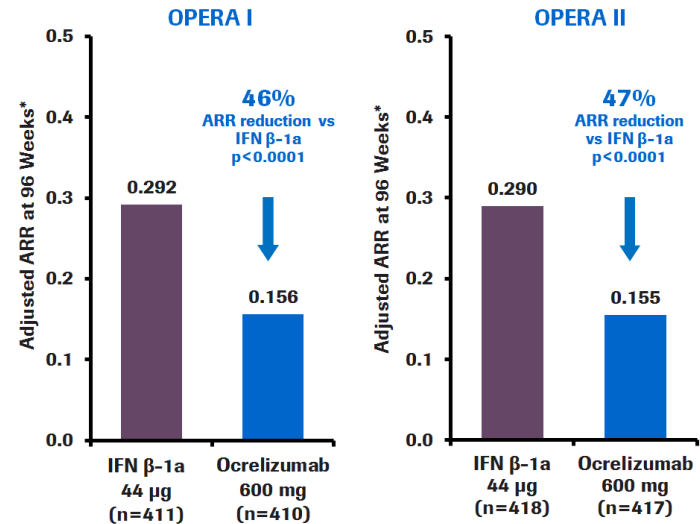
■ Oncology/hematology
 ■ Neuroscience
 ■ Ophthalmology
 ■ Immunology
 ★ FDA Breakthrough Therapy Designation

# OCREVUS: Active in both RMS & PPMS

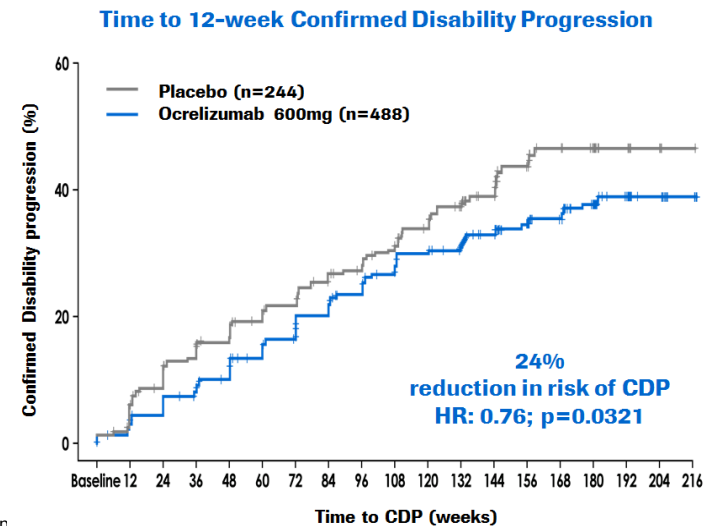


- Selective depletion of a B cell subset leaving the ability to generate new B cells intact
- Administered IV twice yearly

**RMS**



**PPMS**



RMS=relapsing forms of multiple sclerosis (MS) which includes patients with RRMS and SPMS with superimposed PPMS=primary progressive MS;

# Emicizumab: Game changer in hemophilia A



■ Oncology/hematology
 ■ Neuroscience
 ■ Ophthalmology
 ■ Immunology
 ★ FDA Breakthrough Therapy Designation



# Emicizumab addresses major medical needs for both inhibitor and non-inhibitor patients

Emicizumab  
(ACE 910)

NON-INHIBITOR

**On-demand treatment**  
1-3 times/bleeding event, IV

**Prophylaxis treatment**  
3 times/week, IV

Less frequent & SC  
injection

**Inhibiting Factor VIII antibodies in 20-30% of the patients**

INHIBITOR

**Immune Tolerance Induction**  
70-80 % success rate

limitation due to very high cost and heavy burden for patients

No potential to  
induce FVIII inhibitor

**On-demand treatment with  
by-passing agents**  
2-3h intervals, IV

**Prophylaxis with by-passing  
agents**  
Every other day, IV

Potentially more  
effective prophylaxis

**Performance update**

**Innovation and differentiation**

**Improving the standard of care**

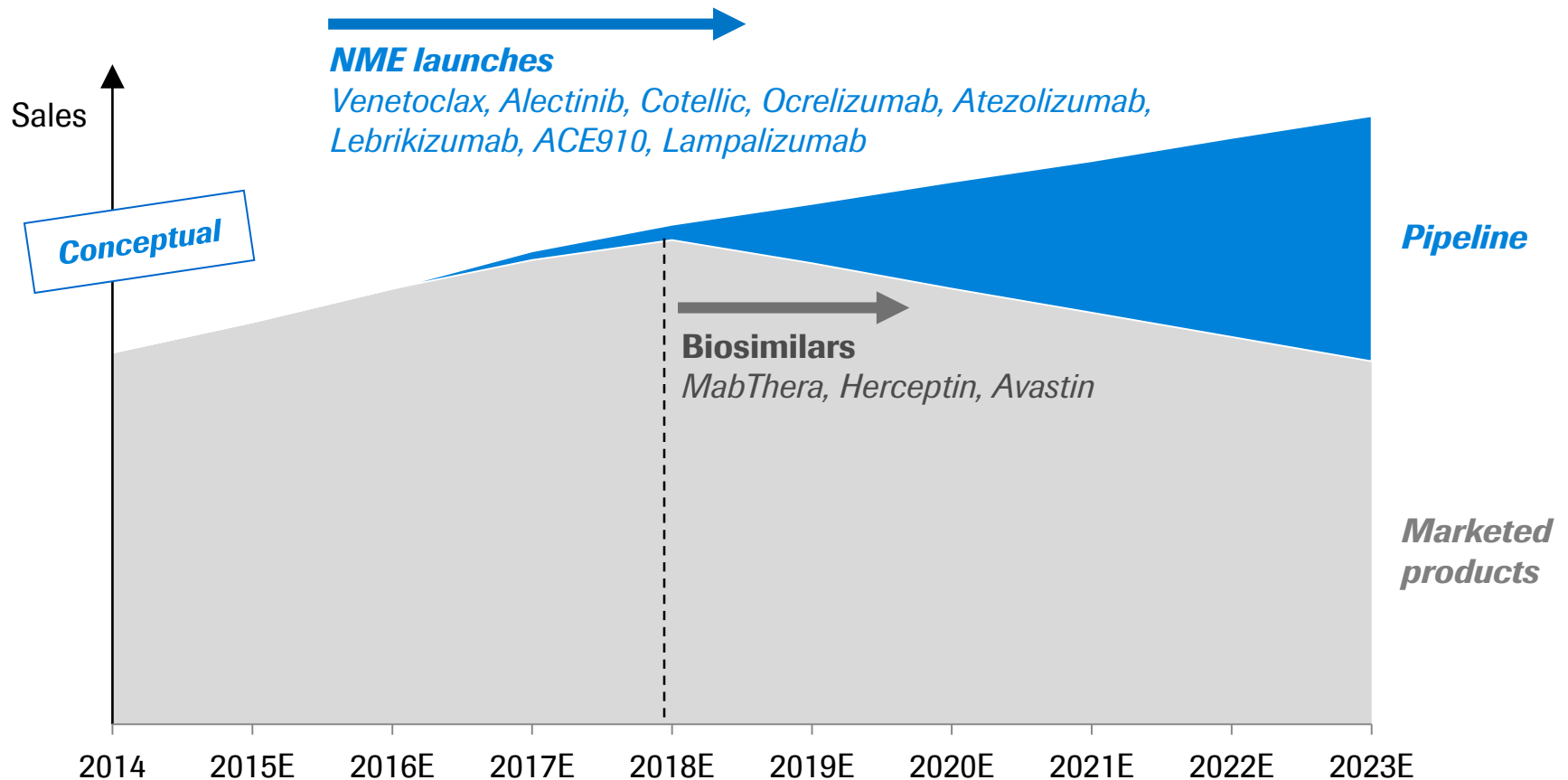
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**Outlook**

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# Positive outlook

## *Strong pipeline mitigates biosimilar impact*



# 2016 outlook

Group sales growth <sup>1</sup>	Low to mid-single digit
Core EPS growth <sup>1</sup>	Ahead of sales growth
Dividend outlook	Further increase dividend in Swiss francs

<sup>1</sup> At Constant Exchange Rates (CER)

*Doing now what patients need next*