Turning innovation into patients benefit

Karl Mahler, Head Investor Relations

Zuerich, August 2016
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Performance update

Innovation and differentiation

Improving the standard of care

Outlook
Q2 2016: Sales growth for fifth consecutive year

All growth rates at Constant Exchange Rates (CER)
HY 2016: Strong core operating profit & margin

+5% at CER

CHFbn

HY 2012: 8.6
HY 2013: 9.5
HY 2014: 9.4
HY 2015: 9.2
HY 2016: 9.9

% of sales

CER=Constant Exchange Rates
Continued leadership in innovation
Launches at historical high

5 NME launches in a year


- Zelboraf
- Erivedge
- PERJETA
- Gazyva
- Kadcyla
- Esbriet
- Cotellic
- Alecensa
- Venclexta
- Tecentriq
- Ocrevus

Roche
Performance update

Innovation and differentiation

Improving the standard of care

Outlook
Roche strategy: Focused on medically differentiated therapies

- Generics
- OTC
- MedTech
- Pharma
- Dia

**Regulators:**
Optimised benefit / risk ratio

**Payors:**
Optimised benefit / cost ratio
Pillars of early R&D
Preserving cultures – increasing collaboration in CIT

Cancer Immunotherapy

OCREVUS
lampalizumab

emicizumab

TECENTRIQ
aOX40
IDOi
aCD20/CD3 TCB
aTIGIT

emactuzumab
aCD40
vanucizumab
aCEA/CD3 TCB
aFAP-IL2v FP
aCEA-IL2v FP

Genentech
A Member of the Roche Group

Roche

CHUGAI
Approach towards innovation

Prioritizing rigorously

We select at late stage entry

…to increase sales potential

Illustrative

Medical need

low

high

Clinical differentiation

low

high

Threshold

Greater differentiation

Sales

Time

Continued

Disqualified
Performance update

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Outlook
2016 onwards: Significant launch activities

Outcome studies are event-driven: timelines may change. Standard approval timelines of 1 year assumed.
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)

UBC=urinary bladder cancer ; PR=partial responses; CR=complete responses
The 7 steps of the cancer immunity cycle guide our prioritization framework for development

1. Release of cancer cell antigens (cancer cell death)
2. Cancer antigen presentation (dendritic cells/ APCs)
3. Priming and activation (APCs & T cells)
4. Trafficking of T cells to tumors (CTLs)
5. Infiltration of T cells into tumors (CTLs, endothelial cells)
6. Recognition of cancer cells by T cells (CTLs, cancer cells)
7. Killing of cancer cells (Immune and cancer cells)
Different tumours show different immune phenotypes and will need different solutions.

**Inflamed**
- CD8+ T cells infiltrated, but non-functional
- Accelerate or remove brakes on T-cell response

**Immune Excluded**
- CD8+ T cells accumulated but not efficiently infiltrated
- Bring T-cells in contact with cancer cells

**Immune Desert**
- 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

**Key Questions:**
- Main barriers?
- Optimally driving both antigen presentation and T cell activation

**Immune Phenotypes:**
- **Immune Desert**
  - CD8+ T cells are absent from tumor and its periphery
- **Immune Excluded**
  - CD8+ T cells accumulated but have not efficiently infiltrated
- **Inflamed**
  - CD8+ T cells infiltrated, but are non-functional

**Key questions:**
- optimally support trafficking of T cells into tumors
- 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

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;

Clinical data within 2 years
## A rich pipeline: Program by tumour type

### Solid tumors

<table>
<thead>
<tr>
<th>Solid tumors</th>
<th>Lung (NSCLC &amp; SCLC)</th>
<th>Breast (TNBC &amp; HER2+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecentriq</td>
<td>Ph1</td>
<td>Ph3</td>
</tr>
<tr>
<td>Tecentriq + chemo ± Avastin</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>Tecentriq + Cotelic</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>aOX40 ± Tecentriq</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>aCEA/CD3 TCB ± Tecentriq</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>IDOi ± Tecentriq</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>emactuzumab ± Tecentriq</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>aCEA-IL2v FP ± Tecentriq</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>aFAP-IL2v FP ± Tecentriq</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>aCD40 ± Tecentriq</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>emactuzumab ± aCD40</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>aCD40 + vanucizumab</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>Tecentriq + vanucizumab</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>aTIGIT ± Tecentriq</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>Tecentriq + daratumumab*</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>Tecentriq + IFN or ipilimumab*</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>Tecentriq + A2Ai*</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>Tecentriq + varilumab*</td>
<td>Ph1</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Melanoma</th>
<th>Lung (NSCLC &amp; SCLC)</th>
<th>Breast (TNBC &amp; HER2+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecentriq + Zelboraf ± Cotelic</td>
<td>Ph1</td>
<td>Ph3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ovarian</th>
<th>Lung (NSCLC &amp; SCLC)</th>
<th>Breast (TNBC &amp; HER2+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecentriq + rucaparib*</td>
<td>Ph1</td>
<td>Ph3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hematological tumors</th>
<th>Lung (NSCLC &amp; SCLC)</th>
<th>Breast (TNBC &amp; HER2+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecentriq + lenalidomide + daratumumab*</td>
<td>Ph1</td>
<td>Ph3</td>
</tr>
<tr>
<td>Tecentriq + azacitidine</td>
<td>Ph1</td>
<td>Ph1</td>
</tr>
<tr>
<td>Tecentriq + Gazyva or +tazemetostat*</td>
<td>Ph1</td>
<td>(R/R FL and DLBCL)</td>
</tr>
<tr>
<td>Tecentriq + Gazyva + polatumumab</td>
<td>Ph2</td>
<td>(R/R FL and DLBCL)</td>
</tr>
<tr>
<td>Tecentriq + Gazyva + lenalidomide</td>
<td>Ph1</td>
<td>(R/R FL and DLBCL)</td>
</tr>
<tr>
<td>Tecentriq + Gazyva + bendamustine or CHOP</td>
<td>Ph1</td>
<td>(1L FL and DLBCL)</td>
</tr>
<tr>
<td>aCD20/CD3 TCB</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>Tecentriq + CD19 CAR-T*</td>
<td>Ph1</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bladder</th>
<th>Lung (NSCLC &amp; SCLC)</th>
<th>Breast (TNBC &amp; HER2+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tecentriq (2L+ UBC)</td>
<td>Ph3</td>
<td></td>
</tr>
<tr>
<td>Tecentriq + BCG (NMIBC)</td>
<td>Ph1</td>
<td></td>
</tr>
<tr>
<td>Tecentriq (2L+ UBC)</td>
<td>Ph3</td>
<td></td>
</tr>
<tr>
<td>Tecentriq + chemo (1L mUC)</td>
<td>Ph3</td>
<td></td>
</tr>
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As of July 21, 2016

= approved; *External collaborations; Other CIT NMEs besides Tecentriq
mNSCL: Treatment allgorism

Efficacy but also safety will play a major role

Strenght of current mono data?
Safety, safety, safety
Convenience

Will PD1 or PDL-1’s be used based on 1st line treatment?

Strenght of combination data?

Patient Number

- mNSCLC incidence: 100%
- mNSCLC 1L drug treated: 60%
- mNSCLC 2L drug treated: 35%
- mNSCLC 3L drug treated: 5%
- I/O mono eligible: 25%
Identify and utilize relevant biomarkers to deliver personalized medicine

Profile predictors of patient response

Predictive Markers of Clinical Benefit

Predictive Markers of Immune Escape

PERSONALIZED PLATFORM

REVERSE TRANSLATION
OCREVUS: First medicine active in RMS and PPMS

- Venclexta: R/R CLL with 17p del
- Cotecitc + Zelboraf: BRAFmut melanoma
- Alecensa: 2L ALK+ NSCLC
- Tecentriq: 2L+ bladder cancer
- Tecentriq: 2/3L lung cancer
- OCREVUS: RMS/ PPMS
- Emicizumab: (ACE910) Hemophilia A
- Lampalizumab: Geographic atrophy
- 2016: Gazyva: R/R iNHL (GADOLIN)
- 2017: Perjeta + Herceptin eBC HER2+ (APHINITY)
- 2018: Tecentriq + Avastin + chemo
  1L NSCLC
- Actemra: Giant cell arteritis (GIACTA)
- Tecentriq + Avastin
  1L RCC
- Alecensa: 1L ALK+ NSCLC

Outcome studies are event-driven: timelines may change. Standard approval timelines of 1 year assumed.
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=relapsing forms of multiple sclerosis (MS) which includes patients with RRMS and SPMS with superimposed relapses; RRMS=relapsing-remitting MS; SPMS=secondary progressive MS; PPMS=primary progressive MS;
Emicizumab: Game changer in hemophilia A

Outcome studies are event-driven: timelines may change. Standard approval timelines of 1 year assumed.
Emicizumab addresses major medical needs for both inhibitor and non-inhibitor patients

<table>
<thead>
<tr>
<th>NON-INHIBITOR</th>
<th>INHIBITOR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>On-demand treatment</strong>&lt;br&gt;1-3 times/bleeding event, IV</td>
<td><strong>On-demand treatment with by-passing agents</strong>&lt;br&gt;2-3h intervals, IV</td>
</tr>
<tr>
<td><strong>Prophylaxis treatment</strong>&lt;br&gt;3 times/week, IV</td>
<td><strong>Prophylaxis with by-passing agents</strong>&lt;br&gt;Every other day, IV</td>
</tr>
</tbody>
</table>

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

**Emicizumab (ACE 910)**

- **Less frequent & SC injection**
- **No potential to induce FVIII inhibitor**
- **Potentially more effective prophylaxis**

Immune Tolerance Induction
70-80 % success rate
limitation due to very high cost and heavy burden for patients
Performance update

Innovation and differentiation

Improving the standard of care

Outlook
Positive outlook

Strong pipeline mitigates biosimilar impact

NME launches
Venetoclax, Alectinib, Cotelpic, Ocrelizumab, Atezolizumab, Lebrikizumab, ACE910, Lampalizumab

Biosimilars
MabThera, Herceptin, Avastin

Sales

Conceptual

Pipeline

Marketed products

## 2016 outlook

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Group sales growth</strong>¹</td>
<td>Low to mid-single digit</td>
</tr>
<tr>
<td><strong>Core EPS growth</strong>¹</td>
<td>Ahead of sales growth</td>
</tr>
<tr>
<td><strong>Dividend outlook</strong></td>
<td>Further increase dividend in Swiss francs</td>
</tr>
</tbody>
</table>

¹ At Constant Exchange Rates (CER)
Doing now what patients need next