Turning science into patient benefits

Alan Hippe, CFO Roche Group

June 2016
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Performance update

Innovation and differentiation

Improving the standard of care

Outlook
Q1 2016: Sales growth for fifth consecutive year

All growth rates at Constant Exchange Rates (CER)
2015: Strong underlying Group Core operating profit & margin

CER=Constant Exchange Rates; * Excluding sale of filgrastim rights in 2014
2015: Dividend and payout ratio further increased

Payout ratio calculated as dividend per share divided by Core earnings per share (diluted); 2015 dividend as proposed by the Board of Directors; Note: For 1995, a special dividend was paid out to mark F. Hoffmann-La Roche’s 100th anniversary in 1996.
Performance update

Innovation and differentiation

Improving the standard of care

Outlook
Roche significantly advancing patient care
Recognition for innovation 2013-present

12 Breakthrough Therapy Designations

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>#</th>
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<tbody>
<tr>
<td>1</td>
<td>Roche</td>
<td>12</td>
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<tr>
<td>2</td>
<td>Novartis</td>
<td>10</td>
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<td>3</td>
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<td>9</td>
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<td>4</td>
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<td>6</td>
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<table>
<thead>
<tr>
<th>Year</th>
<th>Molecule</th>
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<tbody>
<tr>
<td>2016</td>
<td><strong>Ocrelizumab</strong> (PPMS)</td>
</tr>
<tr>
<td></td>
<td><strong>Venclexta</strong> (AML)</td>
</tr>
<tr>
<td></td>
<td><strong>Venclexta + Rituxan</strong> (R/R CLL)</td>
</tr>
<tr>
<td>2015</td>
<td><strong>Actemra</strong> (Systemic sclerosis)</td>
</tr>
<tr>
<td></td>
<td><strong>Tecentriq</strong> (NSCLC)</td>
</tr>
<tr>
<td></td>
<td><strong>Venclexta</strong> (R/R CLL 17p del)</td>
</tr>
<tr>
<td></td>
<td><strong>Emicizumab/ACE 910</strong> (Hemophilia A)</td>
</tr>
<tr>
<td>2014</td>
<td><strong>Esbriet</strong> (IPF)</td>
</tr>
<tr>
<td></td>
<td><strong>Lucentis</strong> (Diabetic retinopathy)</td>
</tr>
<tr>
<td></td>
<td><strong>Tecentriq</strong> (Bladder)</td>
</tr>
<tr>
<td>2013</td>
<td><strong>Alecensa</strong> (2L ALK+ NSCLC)</td>
</tr>
<tr>
<td></td>
<td><strong>Gazyva</strong> (1L CLL)</td>
</tr>
</tbody>
</table>

Source: [http://www.focr.org/breakthrough-therapies](http://www.focr.org/breakthrough-therapies) as at June 2016; PPMS=Primary Progressive Multiple Sclerosis; CLL=Chronic Lymphocytic Leukemia; NSCLC=Non-Small Cell Lung Cancer; IPF=Idiopathic Pulmonary Hypertension
Roche strategy: Focused on medically differentiated therapies

Regulators:
Optimised benefit / risk ratio

Payors:
Optimised benefit / cost ratio
**Approach towards innovation**

*Exploring broad ...*

---

**We invest more early stage**

- **% of budget**
  - **R & Early D**
    - Industry avg: 46%
    - Roche: 54%
  - **Late D**
    - Industry avg: 54%
    - Roche: 60%

---

**...to increase options to choose from**

- **# of NME's entering Pre-clinical**
  - **2012**
    - Industry avg: 11
    - Roche: 19
  - **2013**
    - Industry avg: 18
    - Roche: 19
  - **2014**
    - Industry avg: 19
    - Roche: 19

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*External sources: Investment split based on the CMR Pharmaceutical R&D Factbook (data from 10 companies, 2014); Number of entries into Pre-clinical for Industry based on data from KMR, data for 2011-2013.*
Approach towards innovation
...but prioritizing rigorously

We select at late stage entry

...to increase sales potential

Illustrative

Medical need

低

高

Clinical differentiation

低

高

Threshold

Greater differentiation

Sales

Time

Continued

Disqualified

低

高
Achievements: Innovation
Above-average R&D success rate

Note: Success rates calculated at the project/indication level for overlapping 5-year periods based on KMR data (13 peers and Roche)
Data management

Collaborations are key

Clinical Trials
Controlled, clinical trial data on *expected* benefit and side effects

Clinical Practice
Real outcome data on *actual* benefit and side effects

Analysis

Decisions on treatment
Insight for R&D
Performance update

Innovation and differentiation

Improving the standard of care

Outlook
### New growth opportunities

<table>
<thead>
<tr>
<th>Year</th>
<th>NMEs</th>
<th>Line extensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>Alecensa, Cotellic, Venclexa</td>
<td>Herceptin + Perjeta, Gazyva (GOYA)</td>
</tr>
<tr>
<td>2016</td>
<td>ocrelizumab, Tecentriq, lebrikizumab</td>
<td>Tecentriq + chemo</td>
</tr>
<tr>
<td>2017</td>
<td>ACE910, lampalizumab, olesoxime</td>
<td>Gazyva (GALLIUM)</td>
</tr>
<tr>
<td>Post 2017</td>
<td>gantenerumab, crenezumab, taselisib, etrolizumab</td>
<td></td>
</tr>
</tbody>
</table>

**Therapeutic Areas:**
- Oncology/hematology
- Neuroscience
- Ophthalmology
- Immunology
New growth opportunities

<table>
<thead>
<tr>
<th>NMEs</th>
<th>2015</th>
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<td>Alecensa</td>
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<td>crenezumab</td>
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<tr>
<td>Venclexta</td>
<td>lebrikizumab</td>
<td>olesoxime</td>
<td>taselisib</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>etrolizumab</td>
<td></td>
</tr>
</tbody>
</table>

- **2015**
  - Herceptin + Perjeta
  - Gazyva (GOYA)
- **2016**
  - Tecentriq + chemo
- **2017**
  - Gazyva (GALLIUM)

- **Oncology/hematology**
- **Neuroscience**
- **Ophthalmology**
- **Immunology**
Anti-CD20 franchise
Strategies for long term growth

Protect.. Replace.. Extend..

Medical value

Protect
MabThera
MabThera SC
Rapidly and sustainably convert the market to SC
GALLIUM & await GOYA

Replace
Gazyva

Extend
Gazyva
MabThera SC
Increase medical benefit with Venetoclax in NHL, CLL and expand into new diseases e.g. Multiple Myeloma

Venetoclax in collaboration with AbbVie; SC=subcutaneous; CLL=chronic lymphocytic leukemia; NHL=non-hodgkin’s lymphoma
Third positive readout for Gazyva

**GALLIUM in 1L iNHL**

### CLL11: Ph III Chronic Lymphocytic Leukemia (CLL)

<table>
<thead>
<tr>
<th>1L CLL</th>
<th>Gazyva + chlorambucil</th>
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</thead>
<tbody>
<tr>
<td>n=781</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rituxan + chlorambucil</td>
</tr>
<tr>
<td></td>
<td>chlorambucil</td>
</tr>
</tbody>
</table>

### GADOLIN: Ph III Recurrent Indolent NHL (iNHL)

- **Induction**
  - Rituxan-refractory iNHL
  - n=411
  - Gazyva + bendamustine
  - bendamustine

- **Maintenance**
  - Gazyva q2mo x 2 years

### GALLIUM: Ph III 1L Indolent NHL (iNHL)

- **Induction**
  - 1L iNHL
  - n=1401
  - Gazyva + CHOP or
  - Gazyva + CVP or
  - Gazyva + bendamustine
  - Rituxan + CHOP or
  - Rituxan + CVP or
  - Rituxan + bendamustine

- **Maintenance**
  - Gazyva q2mo x 2 years
  - Rituxan q2mo x 2 years

### GOYA: Ph III 1L Diffuse Large B-cell Lymphoma (DLBCL)

- **Front-line DLBCL**
  - (aggressive NHL)
  - n=1418
  - Gazyva + CHOP
  - Rituxan + CHOP

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Gazyva in collaboration with Biogen Idec; CHOP=Cyclophosphamide, Doxorubicin, Vincristine and Prednisone; CVP=Cyclophosphamide, Vincristine and Prednisolone
Establishing Gazyva as new CD20 backbone

Rituxan sales split by indication

Pie chart shows 2014 Rituxan sales split according to indications; CLL=chronic lymphocytic leukemia; iNHL (FL)=indolent non-hodgkin's lymphoma; aNHL (DLBCL)=aggressive NHL; R/R=relapsed/refractory; Gazyva in collaboration with Biogen Idec
New growth opportunities

NMEs

- Alecensa
- Cotellic
- Venclexta
- Ocrelizumab
- Iebrikizumab
- ACE910
- Lampalizumab
- Olesoxime
- Gantenerumab
- Crenezumab
- Taselisib
- Etrolizumab

Line extensions

- 2015
  - Herceptin + Perjeta
  - Gazyva (GOYA)
- 2016
  - Tecentriq
  - Gazyva (GALLIUM)
- 2017
  - Tecentriq + chemo
- Post 2017

Oncology/hematology
Neuroscience
Ophthalmology
Immunology
CIT portfolio: 10 in-house assets in the clinic

**Antigen presentation**
- ✓ anti-CD40

**Antigen release**
- EGFRi (Tarceva)
- ALKi (Alecensa)
- BRAFi (Zelboraf)
- MEKi (Cotellic)
- anti-CD20 (Gazyva)
- anti-HER2 (Herceptin; Kadryla; Perjeta)
- various chemotherapies
- lenalidomide* (Celgene)
- rociletinib* (Clovis)
- daratumumab* (Janssen)

**T cell Trafficking**

**T cell infiltration**
- anti-VEGF (Avastin)

**T cell killing**
- ✓ Tecentriq (atezolizumab)
- ✓ anti-CSF-1R (emactuzumab)
- ✓ IDOi (NewLink)
- ✓ anti-TIGIT

**Cancer T cell recognition**
- ✓ anti-CEA/CD3 TCB
- ✓ anti-CD20/CD3 TCB

**Priming & activation**
- ✓ anti-CEA-IL2v FP (cergutuzumab amunaleukin)
- ✓ anti-FAP-IL2v FP
- ✓ anti-OX40

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Chen and Mellman. Immunity 2013
NME=new molecular entity; CIT=cancer immunotherapy; FP=fusion protein; TCB=T-cell bispecific
# Atezolizumab: Pivotal programs by disease

## Lung
- FIR and BIRCH
  - Dx+ mono
- POPLAR
  - 2L+ mono
- OAK
  - 2L mono
- IMpower 110
  - 1L non-sq. Dx+ mono

## Bladder
- IMpower 130&150
  - 1L non-sq. combo
- IMpower 111
  - 1L sq. Dx+ mono
- IMpower 131
  - 1L sq. combo
- IMpower 010
  - Adj. Dx+ mono

## Kidney
- IMvigor 210
  - 1L cis-inel. & 2L
- IMvigor 211
  - 2L mono
- IMvigor 010
  - Adj.
- IMmotion 150
  - 1L combo
- IMmotion 151
  - 1L combo

## Breast
- IMpassion 131
  - 1L combo

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**Going deep in diseases where we have strong scientific rationale**

- Rolling filing initiated
- Data in 2016
- Data in 2017
- approved

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cis-inel. = cisplatin ineligible patients
emactuzumab (aCSF-1R); cergutuzumab amunaleukin (aCEA-IL2v FP); vanucizumab (aAng2/VEGF); polatuzumab vediotin (aCD79b ADC); taselisib (PI3Ki); ipatasertib (AKTi); SERD (selective estrogen receptor degrader); idasanutlin (MDM2 antagonist)
May 2016: Combinations in clinical development

Roche NME late stage
Roche NME early stage
Non-Roche apporved drugs

Roche approved drugs
emetuzumab (aCSF-1R); cergutuzumab amunaleukin (aCEA-IL2v FP); vanucizumab (aAng2/VEGF); polatuzumab vediotin (aCD79b ADC); taselisib (PI3Ki); ipatasertib (AKTi); SERD (selective estrogen receptor degrader); idasanutlin (MDM2 antagonist)
New growth opportunities

NMEs

- Alecensa
- Cotellic
- Venclexta

- Ocrelizumab
- Tecentriq
- Ibrutinib

- ACE910
- Lampalizumab
- Olesoxime

Post 2017
- Gantenerumab
- Crenezumab
- Taselisib
- Etrolizumab

Line extensions

- Herceptin + Perjeta
- Gazyva (GOYA)
- Gazyva (GALLIUM)

- Tecentriq + chemo

Pharma Focus:
- Oncology/hematology
- Neuroscience
- Ophthalmology
- Immunology
Ocrelizumab: 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;
Multiple Sclerosis: Improvements over SoC driving market growth

Source: Evaluate Pharma Multiple Sclerosis report, October 2015; * Includes Imusera sales; SoC = standard of care
New growth opportunities

- Alecensa
- ocrelizumab
- ACE910
- crenezumab
- taselisib
- etrolizumab
- Cotellic
- Tecentriq
- lampalizumab
- olesoxime
- gantenerumab
- Venclexta
- lebrikizumab
- Gazyva (GOYA)
- Gazyva (GALLIUM)
- Herceptin + Perjeta
- Tecentriq + chemo
- Gazyva

NMEs

2015
2016
2017
Post 2017

Oncology/hematology
Neuroscience
Ophthalmology
Immunology
Emicizumab (ACE 910) development plan

Non-interventional study expanded to all patients

- Inhibitor study: Enrollment progressing well
- Inhibitor non-interventional study fully recruited (>90 patients) and expanded to non-inhibitors
- Non-inhibitor, pediatric and Q4W dosing studies expected to start in 2016

QW=weekly dosing; Q2W=dosing every 2 weeks; Q4W=dosing every 4 weeks; OLE=open label extension
Performance update

Innovation and differentiation

Improving the standard of care

Outlook
Positive outlook

**Strong pipeline mitigates biosimilar impact**

- **NME launches**: Venetoclax, Alectinib, Cotellic, Ocrelizumab, Atezolizumab, Lebrikizumab, ACE910, Lampalizumab

- **Biosimilars**: MabThera, Herceptin, Avastin

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<th>Year</th>
<th>Sales</th>
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<td>2014</td>
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## 2016 outlook

<table>
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<th>Category</th>
<th>Projection</th>
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<td>Group sales growth(^1)</td>
<td>Mid-single digit</td>
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<tr>
<td>Core EPS growth(^1)</td>
<td>Ahead of sales growth</td>
</tr>
<tr>
<td>Dividend outlook</td>
<td>Further increase dividend in Swiss francs</td>
</tr>
</tbody>
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\(^1\) At constant exchange rates (CER)
Appendix
Roche vision: Personalised reimbursement models

Personalised reimbursement models

1. Pay for performance

2. Multiple-indication pricing

3. Combinations

- Pricing according to benefits delivered to patients in different indications and combinations
- Personalised reimbursement models include:
  - Pay for performance
  - Multiple-indication pricing
  - Combination pricing
Pay for performance

“Level of reimbursement based on a patient’s response to a medicine over a specified time period”

AIFA - Payment by Results procedure

Start of the new treatment in all eligible patients

- Evaluation after x days/cycles
  - NON-RESPONDERS
    - Treatment is stopped
    - The overall patient’s cost of treatment is not reimbursed
    - Pay-back by Market Authorization Holder to public hospital
  - RESPONDERS
    - Treatment is continued
    - Treatment is reimbursed by NHS

(+) - Fair reimbursement for patients on an individual level

(-) - Only a few healthcare systems technically support reimbursement at patient level

- Which outcome is important?

Non responders defined as disease progression or progression-related death, unacceptable toxicity not allowing continuation of treatment or toxicity-related death

Source: Managed Entry agreements for pharmaceuticals. The European experience – LSE April 2013
The obligation and rules to report adverse events (AE) applies equally for treatments registered in the AIFA registry according to the national pharmacological requirements.
Multiple-indication pricing

“Allows a medicine approved in different indications and combinations to be priced according to benefits delivered in each indication and combination”

**Now** – unit of drug has same price across all indications

- All indications
- List price (invoice price)

**Future** – single or combination drug price varies by indication based on benefit

- Indication A ➔ Price X
- Indication B ➔ Price Y
- Indication C ➔ Price Z
- Other ➔ Price X

**(+)**
- Best reflects reality of current treatment paradigms, particularly in oncology

**(-)**
- Requires drug-utilisation tracking substantial at patient level
Combination pricing

“Ensures benefits of combination therapies are reflected while considering the limits of healthcare budgets”

**Now** – unit of drug has same price, whether used as single agent or in combination

- Single use or combination
- List price product A (invoice price)
- List price product B (invoice price)

**Future** – price varies by single or combination use based on benefit

- Product A
- Product B
- Product A + B (without PRM)
- Product A + B (with PRM)
- Price X
- Price Y
- Price Z
- Potential Price

**(+)**
- Addresses the reality of combination treatments, particularly oncology
- Takes healthcare budget into consideration

**(-)**
- Not all drug combos are from the same company
- High complexity with many possible combinations
Doing now what patients need next