Improving the standard of care

Severin Schwan, CEO Roche Group

London, September 2015
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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

Improving the standard of care

Outlook
Q2 2015: Sales growth for fifth consecutive year

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

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<td>8.3 CHFbn</td>
<td>8.6 CHFbn</td>
<td>9.5 CHFbn</td>
<td>9.4 CHFbn</td>
<td>9.2 CHFbn</td>
</tr>
</tbody>
</table>

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

Dividend payout ratio (%)

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

Improving the standard of care

Outlook
Roche strategy: Focused on medically differentiated therapies

**Regulators:**
Optimised benefit / risk ratio

**Payors:**
Optimised benefit / cost ratio
Progressing in Personalised Healthcare
60% of phase 2 & 3 products have PHC component

<table>
<thead>
<tr>
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Progressing in Personalised Healthcare
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- Oncology
- Immunology
- Infectious Diseases
- Neuroscience
- Ophthalmology
- Molecular Diagnostics
- Tissue Diagnostics
- Professional Diagnostics
The 7 steps of the Cancer-Immunity Cycle guide our prioritization framework for Atezolizumab

Step 1: Release of Cancer Cell antigens:
- ex: Atezo + chemo, Gazyva, aCD40

Step 2 & 3: Cancer antigen presentation & priming and activation
- ex: Atezo + interferon, OX40

Steps 4 & 5: Trafficking & infiltration of T cells to tumours
- ex: Atezo + Avastin, aCSF1R,

Steps 6 & 7: Recognition of cancer cells by T cells & killing of cancer cells
- ex: Atezo + Meki, IDOi, aOX40

Chen and Mellman. Immunity 2013
Leverage diagnostics to rapidly launch atezolizumab

Diagnostic selection for atezo with best-in-class Dx

Leapfrog competition into 1L via first in class combinations

Rapidly entrench a new standard of care: Combinations with Chemo or Avastin in 1L

Personalize cancer immunotherapy

Identify patients for best combinations by biomarker discovery and development
Atezolizumab biomarker development
*Toward best-in-class PDL1 diagnostic

PDL1 expression on immune cells (IC) and tumor cells (TC):

- Immune cell staining
- Tumor cell staining

Assessed using a sensitive and specific proprietary monoclonal antibody assay* developed by Ventana in collaboration with Pharma

Gettinger S. et al, ASCO 2015
Atezolizumab in 2/3L NSCLC (POPLAR)

OS benefit correlates with PD-L1 expression

**N = 287**

- TC3 or IC3 (16%)*: HR = 0.46
- TC2/3 or IC2/3 (37%)*: HR = 0.56
- TC1/2/3 or IC1/2/3 (68%)*: HR = 0.63
- TC0 and IC0 (32%)*: HR = 1.12

**PFS**

- TC3 or IC3 (16%)*: HR = 0.57
- TC2/3 or IC2/3 (37%)*: HR = 0.70
- TC1/2/3 or IC1/2/3 (68%)*: HR = 0.87

- TC0 and IC0 (32%)*: HR = 1.17

**In favor of atezolizumab**

**In favor of docetaxel**

- Biomarker identifies patients most likely to benefit from atezolizumab
- PD-L1 negative patients seem to benefit rather from the standard chemo

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*a* = Unstratified HR; * = eligible patient population

Spira A. et al, ASCO 2015
Roche Cancer Immunotherapy
Scientifically driven strategy

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Personalize cancer immunotherapy

Identify patients for best combinations by biomarker discovery and development
**Cancer Immunotherapy**

*Will be a mix of single agent and combinations*

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**Inflamed**

- **Can responses be improved?**

**Non-inflamed**

- **Can we convert these to responsive?**

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**Tumor phenotype by T cell staining**

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**20-30% patients**

- T cells present in tumor
- Chemokines present (attract leukocytes)

---

**70-80% patients**

- Lack lymphocytic infiltrates

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**Responsive to single agent immunotherapies**

**Non-responsive to single agent immunotherapies**
Atezolizumab + chemotherapy combinations

Example 1: Lung cancer: first/best-in-class potential

- Preliminary data; ~25 patients will be included in each arm for final analysis

<table>
<thead>
<tr>
<th>Arm C, n=8</th>
<th>Arm D, n=17</th>
<th>Arm E, n=16</th>
</tr>
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<tbody>
<tr>
<td><strong>Atezolizumab + carboplatin/paclitaxel</strong></td>
<td><strong>Atezolizumab + carboplatin/pemetrexed</strong></td>
<td><strong>Atezolizumab + Carboplatin/nab-paclitaxel</strong></td>
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<tr>
<td><strong>ORR</strong> (95% CI)</td>
<td><strong>50% (15.7-84.3)</strong></td>
<td><strong>76.5% (50.1-93.2)</strong></td>
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</table>

ORR across all arms = 63.4% (46.9-77.9)

CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease
Atezolizumab + Avastin combination

Example 2: Kidney Cancer

Increased T-cell infiltrate in biopsies while on-treatment

Early response rate data promising, regardless of PDL1 status

Phase 2 in RCC ongoing (n= 300); Phase 3 initiated

Sznol et al. ASCO GU 2015
Roche Cancer Immunotherapy
Scientifically driven strategy

Leverage diagnostics to rapidly launch atezolizumab

Diagnostic selection for atezo with best-in-class Dx

Leapfrog competition into 1L via first in class combinations

Rapidly entrench a new standard of care: Combinations with Chemo or Avastin in 1L

Personalize cancer immunotherapy

Identify patients for best combinations by biomarker discovery and development
Biomarker discovery and development

Integral part of the cancer immunotherapy R&D

Our comprehensive biomarker platform:

- **Protein-Expression**
  - PDL1, other CI targets
  - Multiplex IHC

- **DNA-Mutation & CNVs**
  - Ex: EGFR, BRAF
  - DNA Sequencing

- **mRNA-Expression**
  - Cell signatures, targets
  - RNA Sequencing

Research
(gRED, pRED, Chugai & external)

Development
(early and late)

Immunotherapy

Clinical Insights & Biomarkers
(Internal and External)
Clinical immunotherapy program keeps growing

**Phase I**
- aPDL1: Solid tumors
- aPDL1 + chemo: Solid tumors
- aPDL1 + Tarceva: NSCLC
- aPDL1 + Zelboraf: Melanoma
- aPDL1 + cibimetinib: Solid tumors
- aPDL1 + Avastin: NSCLC
- aPDL1 + Gazyva: R/R FL / aNHL
- aPDL1 + Avastin + chemo: Solid tumors
- aPDL1 + lenalidomide: MM
- aPDL1 + Zelboraf + cobi: Melanoma
- aCSF-1R: Solid tumors
- aCEA-IL2v FP: Solid tumors
- aOX40: Solid tumors
- aCEA/CD3 TCB: Solid tumors

**Phase II**
- aPDL1: Solid tumors
- aPDL1 + ipilimumab: Solid tumors
- aPDL1 + IFN-alfa: Solid tumors
- aPDL1 + aCD40: Solid tumors
- aPDL1 + aOX40: Solid tumors
- aPDL1 + aCSF-1R: Solid tumors
- aPDL1 + aCEA-IL2v FP: Solid tumors
- aPDL1 + IDO: Solid tumors
- aPDL1 + chemo: Solid tumors
- aPDL1 + Avastin + chemo: Solid tumors
- aPDL1 + Zelboraf + cobi: Melanoma
- aCSF-1R: Solid tumors
- aCEA-IL2v FP: Solid tumors
- aOX40: Solid tumors
- aCEA/CD3 TCB: Solid tumors

**Phase III**
- aPDL1: 2/3L NSCLC
- aPDL1 + Avastin: 1L Renal
- aPDL1 + chemo: 1L non sq NSCLC
- aPDL1 + Avastin + chemo: 1L non sq NSCLC
- aPDL1 + chemo: 1L sq NSCLC
- aPDL1: 1L non sq NSCLC (Dx+)
- aPDL1: 1L sq NSCLC
- aPDL1: 1L TNBC
- aPDL1 + Avastin: 1L RCC
- aPDL1 + Avastin: Adjuvant MIHC (Dx+)
- aPDL1: Adjuvant NSCLC

Status as at June 30, 2015

Data at ASCO 2015

Additions in 2015

2015 readout expected
Progressing in Personalised Healthcare

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Infectious Diseases
Neuroscience
Ophthalmology

Molecular Diagnostics
Tissue Diagnostics
Professional Diagnostics

Roche
**Ocrelizumab: Phase 3 meets endpoints vs. SOC**

**Results confirm central role of B cells in MS**

<table>
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<tr>
<th>Study Endpoint</th>
<th>Reduction versus Rebif®</th>
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<tr>
<td><strong>Primary</strong></td>
<td></td>
</tr>
<tr>
<td>Annualized Relapse Rate</td>
<td>✓</td>
</tr>
<tr>
<td>Confirmed Disability Progression</td>
<td>✓</td>
</tr>
<tr>
<td>MRI endpoints</td>
<td>✓</td>
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**Targeted product profile**
- Humanized antibody targeting CD20+ B cells
- Selective depletion of a subset of B cells leaving the ability to generate new B cells intact
- Administered by IV twice yearly

**Phase 3 OPERA I/II results in RMS**
- Superiority vs. Rebif® (Interferon beta-1a) on primary and major secondary endpoints achieved
- Adverse events (including serious infections) similar to Rebif®
- Data to be presented at ECTRIMS

SOC=standard of care; MS=multiple sclerosis; RMS=relapsing forms of MS; Rebif® (Interferon beta-1a)
Performance update

Improving the standard of care

Outlook
Roche: 6 new molecular entities (NMEs) for near-term readout

<table>
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<th>2015</th>
<th>2016</th>
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<tr>
<td><strong>Alectinib</strong> (filing)</td>
<td><strong>Atezolizumab</strong> (aPDL1) Lung and bladder (filings)</td>
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<td><strong>Venetoclax</strong> (filing)</td>
<td><strong>Ocrelizumab</strong> (filing)</td>
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<td><strong>Cobimetinib / Zelboraf</strong> (approval)</td>
<td><strong>Lebrikizumab</strong> (filing)</td>
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Planned key data presentations in H2 2015

Vienna, 25-29 Sep

Atezolizumab
- UBC: IMvigor 210 Ph II\(^1\)
- NSCLC: POPLAR Ph II\(^1,2\)
- NSCLC: BIRCH Ph II\(^1\)
- NSCLC: Chemo combos update\(^2\)

Alectinib
- ALK+NSCLC: Ph II update\(^2\)

Barcelona, 7-10 Oct

Ocrelizumab
- RMS: OPERA I / II Ph III

San Francisco, 18-21 Nov

Atezolizumab
- Melanoma: Combo with Zelboraf Ph Ib
  (abstracts submitted)

Cobimetinib + Zelboraf
- BRAF+Melanoma: coBRIM efficacy update
  (abstracts submitted)

San Antonio, 8-12 Dec

Atezolizumab
- TNBC: Combo with abraxane Ph Ib
  (abstracts submitted)

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\(^1\) “Data not yet in-house; planned to be submitted to an up-coming congress”;
\(^2\) Potentially at World Conference on Lung Cancer (WCLC) 2015

UBC=Urinary Bladder Cancer; NSCLC=Non-Small Cell Lung Cancer; RMS=Relapsing forms of Multiple Sclerosis;
TNBC=Triple Negative Breast Cancer
## 2015 outlook

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<th>Category</th>
<th>Description</th>
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<tr>
<td>Group sales growth(^1)</td>
<td>Low to mid-single digit</td>
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<tr>
<td>Core EPS growth(^1)</td>
<td>Ahead of sales growth(^2)</td>
</tr>
<tr>
<td>Dividend outlook</td>
<td>Further increase dividend in Swiss francs</td>
</tr>
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\(^1\) At constant exchange rates

\(^2\) Excluding sale of filgrastim rights in 2014
Doing now what patients need next