Improving the standard of care

Severin Schwan, CEO Roche Group

Bernstein Strategic Conference
New York, May 2015
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2. legislative and regulatory developments and economic conditions;
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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
Q1 2015: Sales growth for 5\textsuperscript{th} consecutive year

All growth rates at Constant Exchange Rates (CER)
2014: Group core operating profit & margin remains at high levels

CER=Constant Exchange Rates

* Excluding one-time double charge for the US Branded Prescription Drug fee in 2014
2014: Dividend and payout ratio further increased

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

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- **Oncology**
- **Immunology**
- **Infectious Diseases**
- **Neuroscience**
- **Ophthalmology**
- **Molecular Diagnostics**
- **Tissue Diagnostics**
- **Professional Diagnostics**
Progressing in Personalised Healthcare
60% of phase 2 & 3 products have PHC component

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Oncology | Immunology | Infectious Diseases | Neuroscience | Ophthalmology

Molecular Diagnostics | Tissue Diagnostics | Professional Diagnostics
Roche Cancer Immunotherapy
Encouraging early PD-L1 data in monotherapy

Range across various studies

<table>
<thead>
<tr>
<th>NSCLC 2L</th>
<th>ORR range</th>
<th>mPFS range</th>
<th>mOS* range</th>
<th>Prevalence</th>
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</thead>
<tbody>
<tr>
<td>Un-stratified</td>
<td>~ 15%</td>
<td>~ 3 m</td>
<td>~ 9-11 m</td>
<td>~ 15%</td>
</tr>
<tr>
<td>Stratified</td>
<td>40-45%</td>
<td>~ 6-8 m</td>
<td>Not reached</td>
<td>~20-30%</td>
</tr>
</tbody>
</table>

Range across various studies

<table>
<thead>
<tr>
<th>Bladder 2L</th>
<th>ORR range</th>
<th>mPFS range</th>
<th>mOS range</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stratified</td>
<td>25-50%</td>
<td>~ 2-5.5 m</td>
<td>Not reached</td>
<td>~30%</td>
</tr>
</tbody>
</table>

* Comparisons based on publicly available competitor data sets. Significant limitations with these cross-trial comparisons; significant variability in baseline population demographics further limit conclusions.
Note: CheckMate 057 2L+ non-squamous NSCLC trial was stopped early because the study met its OS endpoint.
Roche Cancer Immunotherapy
What next?

→ Better patient stratification by more sophisticated biomarker analysis

→ Treating unresponsive tumours by new combination therapies
Roche Cancer Immunotherapy
Better biomarker analysis

*Evaluate tumor: Is the tumor inflamed?

Yes

1. Strong PDL1
   - Tx with aPDL1/PD1

2. Weak PDL1
   - Are suppressive myeloid cells present? CSF1R?

3. No PDL1
   - IDO/kynuretinin expressed?

No

1. Are T cells at tumor periphery?

2. MHC loss?

3. No T cells?
   - T cell bispc or CAR-T
     - Attempt to stimulate anti-cancer immunity:
       - Anti-OX40
       - Anti-CD40
       - Anti-CTLA4
       - Cancer vaccine
       - Any of the above with Anti-PDL1 or Anti-PD1

*Hypothetical algorithm
Roche Cancer Immunotherapy
Partnership with Foundation Medicine

Molecular monitoring

Patient care

Clinical decision

R&D insights

Clinical decision

Roche Cancer Immunotherapy
Partnership with Foundation Medicine
Roche Cancer Immunotherapy

**PD-L1 + chemo in 1L NSCLC (Ph1)**

<table>
<thead>
<tr>
<th>Response, n (%)</th>
<th>Arm C (n = 5)</th>
<th>Arm D (n = 12)</th>
<th>Arm E (n = 13)</th>
<th>All (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR (95% CI)</strong></td>
<td>3 (60%) (19-92)</td>
<td>9 (75%) (45-93)</td>
<td>8 (62%) (33-83)</td>
<td>20 (67%) (48-82)</td>
</tr>
</tbody>
</table>

CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease

Liu S. et al, ASCO 2015
Roche Cancer Immunotherapy

**Broad program with PD-L1**

**Dx + Monotherapy**

**Examples:**
- mRCC (Ph II)
- mUBC (Ph II)
- 2L mNSCLC (Ph II ‘BIRCH’, ‘POPLAR’, ‘FIR’, Ph III ‘OAK’)
- Dx+ 1L NSCLC (2x: Sq/NSq, Ph III)
- Dx+ mUBC (Ph III)

**Immune Doublets**

**Examples:**
- Loc adv/ metastatic solid tumours with ipilimumab or Interferon alfa-2b (Ph Ib)
- Combination with CSF-1R (Ph Ib)
- Combination with anti-CD40 (Ph Ib)
- Combination with Incyte’s IDOi (Ph Ib)
- Combination with anti-OX40 (Ph Ib)
- Combination with CEA-IL2v (Ph Ib)
- Combination with Celldex anti-CD27

**Chemotherapy Combinations**

**Examples:**
- 1L NSCLC Squamous and Non-Squamous with platinum doublets (x3, Ph III)
- 1L TNBC with Abraxane (Ph III)

**Targeted Therapy Combinations**

**Examples:**
- mRCC with Avastin (Ph II)
- mRCC with Avastin (Ph III)
- EGFR+ NSCLC w/Tarceva (Ph Ib)
- ALK+ NSCLC w/alectinib (Ph Ib)
- Solid tumours with Avastin (Ph Ib)
- Solid tumors w/cobimetinib (Ph Ib)
- Lymphoma with Gazyva (Ph Ib)
- HER2+ with Herceptin, Kadcyla, Perjeta (multi-arm, Ph Ib)
# Roche Cancer Immunotherapy

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
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<tbody>
<tr>
<td>PDL1 + Tarceva NSCLC</td>
<td>OX40</td>
<td>PDL1 NSCLC (Dx+)</td>
</tr>
<tr>
<td>PDL1 + Zelboraf Melanoma</td>
<td>CEA CD3</td>
<td>PDL1 2/3L NSCLC</td>
</tr>
<tr>
<td>PDL1</td>
<td>IDO</td>
<td>PDL1 + Avastin 1L Renal</td>
</tr>
<tr>
<td>PDL1 + Avastin Solid tumors</td>
<td>PDL1 + OX40**</td>
<td>PDL1 1/2L Bladder</td>
</tr>
<tr>
<td>PDL1 + cobi Solid tumors</td>
<td>PDL1 + CSF-TR**</td>
<td></td>
</tr>
<tr>
<td>PDL1 + ipilimumab Solid tumors</td>
<td>PDL1 + CEA IL2v**</td>
<td></td>
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<tr>
<td>PDL1 + IFN-alfa Solid tumors</td>
<td>PDL1 + Zelboraf + cobi**</td>
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<tr>
<td>PDL1 + CD40 Solid tumors</td>
<td>PDL1 + lenalidomide** MM</td>
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<tr>
<td>PDL1 + Avastin + FOLFOX CRC</td>
<td>PDL1** tba</td>
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<td>PDL1 + Gazyva Blood cancer</td>
<td>PDL1** tba</td>
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<td>PDL1 TNBC</td>
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<td>Solid tumors</td>
<td>NME** tba</td>
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## Status as at May 31, 2015

- ** Anti-PDL1 trials
- NMEs monotherapy
- Immune doublets
- ** Study start in 2015
- Data at ASCO 2015

### Data at ASCO 2015

- PDL1 + Avastin
- PDL1 + Tarceva
- PDL1 + Zelboraf
- PDL1 + lenalidomide MM
- PDL1 + chemo
- PDL1 + ifn-alfa
- PDL1 + ipilimumab
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Oncology | Immunology | Infectious Diseases | Neuroscience | Ophthalmology
Molecular Diagnostics | Tissue Diagnostics | Professional Diagnostics

Tarceva®
Zelboraf®
Erivedge®
Rituxan®
Gazyva®
Herceptin®
Perjeta®
Kadcyla®
Avastin®
Xeloda®
Esbriet®
Pulmozyme®
Xolair®
Actemra®
Lucentis®
Looking for the next step in Multiple Sclerosis therapy

Relative reduction in Annualized Relapse Rate (ARR)

- Trial durations vary from 6 mos. to 3 yrs; studies included different patient populations, different in/exclusion criteria, different ARR definitions and data were collected over a time span of more than 20 years.
**Progressing in Personalised Healthcare**

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### Marked Products

- Oncology
- Immunology
- Infectious Diseases
- Neuroscience
- Ophthalmology

### Diagnostics

- Molecular Diagnostics
- Tissue Diagnostics
- Professional Diagnostics
- Professional Diagnostics
ACE 910 in Hemophilia A
A novel FVIIIa mimetic bispecific antibody

Current Treatments

Non-Inhibitor Patients

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

Inhibiting Factor VIII antibodies in 20-33% of the patients

Inhibitor Patients

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

- On-demand treatment with bypassing agents 2-3h intervals, IV
- Prophylaxis with bypassing agents Every other day, IV

Benefit ACE 910

- Less frequent dosing
- Subcutaneous

- Potential new treatment option

In collaboration with Chugai
Performance update

Improving the standard of care

Outlook
# ASCO 2015: Roche highlights

## Skin cancer
- **cibimetinib + Zelboraf**: Ph III *(coBRIM)* in 1L BRAF+ mM; PFS & biomarker update
- **cibimetinib + Zelboraf**: Ph Ib *(BRIM7)* in BRAF+ mM; OS update

## Lung cancer
- **alectinib**: two Ph II in 2L ALK+ NSCLC
- **Anti-PDL1**: POPLAR, COMBO, FIR
- **Avastin**: mesothelioma

## Bladder cancer
- **Anti-PDL1**: Ph I update in bladder

## Breast cancer
- **Kadcyla**: Ph II *(ADAPT)* neoadjuvant 12 weeks HER2+ HR+ BC
- **Kadcyla + Perjeta**: Ph III *(MARIANNE)* in 1L HER2+ mBC
- **Herceptin + Perjeta**: Ph II *(NEOPSHERE)* in neoadjuvant HER2+ BC
- **Avastin + Letrozole**: Ph III *(CALGB40503)* in 1L HER2+ BC

## Hematology
- **Gazyva**: Ph III *(GADOLIN)* in R/R iNHL
- **Venetoclax**: Ph I in R/R NHL and R/R MM

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Collaborations: Zelboraf with Plexikon; Cobimetinib with Exelixis; Alectinib with Chugai, Gazyva with Biogen Idec; Kadcyla with ImmunoGen
## 2015 outlook

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<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>
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<td>Dividend outlook</td>
<td>Further increase dividend in Swiss francs</td>
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\(^1\) At constant exchange rates  
\(^2\) Excluding sale of filgrastim rights in 2014
Doing now what patients need next