Innovation and differentiation

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Performance update

Innovation matters: Industry in context

Building pillars of innovation and growth

Summary
Group: Continued strong sales growth

All values at constant exchange rates

Excluding 340B sales reserves release
Group growth supported by all regions

All values at constant exchange rates
Roche: Increase in operating profit & margin

Group core operating profit (CHF bn) and margin

<table>
<thead>
<tr>
<th>Year</th>
<th>Operating Profit (CHF bn)</th>
<th>Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>HY 2009</td>
<td>8.40</td>
<td>35.0%</td>
</tr>
<tr>
<td>HY 2010</td>
<td>9.16</td>
<td>37.2%</td>
</tr>
<tr>
<td>HY 2011</td>
<td>8.25</td>
<td>38.1%</td>
</tr>
<tr>
<td>HY 2012</td>
<td>8.64</td>
<td>38.5%</td>
</tr>
<tr>
<td>HY 2013</td>
<td>9.49</td>
<td>40.7%</td>
</tr>
</tbody>
</table>

+10% at CER

CER = Constant Exchange Rates
Roche strategy: Focused on medically differentiated therapies

Regulators:
Optimised benefit / risk ratio

Payors:
Optimised benefit / cost ratio
Performance update

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Summary
Pharma market drivers and constraints

*Balance of these factors will determine future growth*

- Major advances in science and medicine
- Growth and aging of world population
- Increasing wealth and access in Emerging Markets

- Patent expirations
- Global economic slowdown
  - Slower expansion of budgets in emerging markets
  - Increased pricing hurdles in developed world
Access and pricing: Challenges and opportunities

Behavior stratified into 3 geographic clusters

**Developed world ex-US**
(37% of world market, 10% of population)
- Payers determine price

**Emerging Markets**
(28% of world market, 85% of population)
- Spend limited by GDP per capita

**United States**
(35% of world market, 5% of pop)
- Free, stable pricing

- **Access and pricing: Challenges and opportunities**
- **Behavior stratified into 3 geographic clusters**

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UK: Innovation recognized for products with high medical benefit

NICE recommendations

Medical benefit

<table>
<thead>
<tr>
<th>Medical benefit</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>40%</td>
<td>60%</td>
<td>100%</td>
</tr>
<tr>
<td>Restricted</td>
<td>40%</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>20%</td>
<td>20%</td>
<td></td>
</tr>
</tbody>
</table>
Segregation will continue as only true innovation will be rewarded
Performance update

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Summary
Roche: R&D well balanced from a risk & disease point of view

Industry average probability of success – Phase I to Registration

Source: Bernstein Equity Research, Tufts University and Roche analysis
## Where science takes us

### Oncology
- **Launched**
  - Avastin
  - MabThera
  - Herceptin
  - Xeloda
  - Tarceva
  - Zelboraf
  - Erivedge
  - Perjeta
  - Kadcyla
  - MetMab
- **Phase III**
  - anti-PDL1
  - BCL2i
  - GA101
  - cobimetinib (MEKi)
- **Phase II**
  - 10 phase II

### Immunology/Inflammation
- **Launched**
  - etrolizumab
  - Mabthera RA
  - Actemra
  - Lucentis
  - Xolair
- **Phase III**
  - lebrikizumab²
  - lampalizumab²
- **Phase II**
  - 2 phase II

### Neuroscience
- **Launched**
  - bitopertin
  - ocrelizumab
  - gantenerumab
- **Phase III**
  - 3 Phase III
- **Phase II**
  - 4 phase II

**Strong and growing**

**Strongly emerging**

**Earlier stage**

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¹ FPI expected 1H 2014; ² Phase III decision pending
YTD/ 09 2013: Many positive moves into late stage since beginning of the year

1. **etrolizumab**
   - UC and CD

2. **lebrikizumab**
   - asthma

3. **gantenerumab**
   - Alzheimer's

4. **ocrelizumab**
   - MS

5. **bitopertin**
   - schizophrenia

6. **Bcl-2i (GDC 0199)**
   - hem. cancers

7. **anti-PDL1**
   - solid tumours

8. **cobimetinib (MEKi)**
   - melanoma

9. **onartuzumab (MetMAb)**
   - NSCLC

10. **obinutuzumab (GA101)**
    - CLL

11. **Kadcyla (EU)**
    - HER2+ BC

**Phase III decision pending**

1. **alectinib (ALKi)**
   - NSCLC

2. **lampalizumab**
   - geographic atrophy

**Data readout**

1. **mGlu2**
   - treatment-resistant depression

2. **mGlu5**
   - treatment-resistant depression

3. **crenezumab**
   - Alzheimer's

4. **CD22/CD79b ADC**
   - hem. cancers

5. **anti-EGFL7**
   - solid tumours

6. **PI3 kinase**
   - solid tumours

7. **dual PI3 kinase/mTOR**
   - solid tumours

**Partnering options**

1. **HCV DAA**
   - HepC

2. **inclacumab (P selectin)**
   - ACS/CVD

3. **anti-PCSK9**
   - metabolic diseases

**Ph III NMEs**

1. **Ph II/III label enabling**

- Moved to phase III

- Oncology
- Neuroscience
- Immunology
- Ophthalmology
- Virology
- Metabolism
Personalized Healthcare to optimize treatment
Emerging in non-oncology indications

- **gantenerumab**
  Alzheimer
  *(CSF1 β-amyloid)*

- **bitopertin**
  Schizophrenia
  *(CFHR12)*

- **crenezumab**
  Alzheimer
  *(multiple targets)*

- **lampalizumab**
  Geographic atrophy
  *(not disclosed)*

- **lebrikizumab**
  Asthma
  *(periostin level)*

- **etrolizumab**
  Inflammatory bowel disease
  *(not disclosed)*

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1 CSF=cerebrospinal fluid; 2 CFHR1=Complement factor H-related protein 1
Anti-Factor D

Ophthalmology
Lampalizumab

High medical need - Geographic Atrophy (GA)

AMD (Drusen) → Extrafoveal GA → Advanced GA
Lampalizumab: Anti-factor D

**High efficacy in subpopulation with exploratory biomarker**

- GA progression rate decreased by 44% at 18 months.
- In the subset of patients with better vision (20/50 to 20/100), progression was reduced by 54%
- All comers: 20.4% reduction rate at 18 months

**Safety**

- No unexpected or unmanageable SAEs
- Intraocular inflammation AE rates and intraocular pressure elevation AE rates were consistent with Lucentis rates in wAMD

MAHALO study, presented at ASRS 2013, SAE= Serious Adverse Events
Anti-PDL1

Immunotherapy
Tumor PD-L1 enables cancer immune evasion
Anti-PDL1 inhibits binding of PD-L1 to PD-1 and B7.1
### MPDL3280A Phase Ia in NSCLC: Best response by PD-L1 IHC Status

<table>
<thead>
<tr>
<th>Diagnostic Population(^a) (n = 53)</th>
<th>ORR(^b) % (n/n)</th>
<th>PD Rate % (n/n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHC 3</td>
<td>83% (5/6)</td>
<td>17% (1/6)</td>
</tr>
<tr>
<td>IHC 2 and 3</td>
<td>46% (6/13)</td>
<td>23% (3/13)</td>
</tr>
<tr>
<td>IHC 1/2/3</td>
<td>31% (8/26)</td>
<td>38% (10/26)</td>
</tr>
<tr>
<td>All Patients(^c)</td>
<td>23% (12/53)</td>
<td>40% (21/53)</td>
</tr>
</tbody>
</table>

\(^a\) IHC 3: ≥ 10% tumor immune cells positive for PD-L1 (IC+); IHC 2 and 3: ≥ 5% tumor immune cells positive for PD-L1 (IC+); IHC 1/2/3: ≥ 1% tumor immune cells positive for PD-L1 (IC+); IHC 0/1/2/3: all patients with evaluable PD-L1 tumor IC status.

\(^b\) ORR includes investigator-assessed unconfirmed and confirmed PR.

\(^c\) All patients includes patients with IHC 0/1/2/3 and 7 patients have an unknown diagnostic status. Patients first dosed at 1-20 mg/kg by Oct 1, 2012; data cutoff Apr 30, 2013.

*Soria et al, ECCO 2013*
Duration of treatment in responders

Sustained response in majority of responders

<table>
<thead>
<tr>
<th>Histology</th>
<th>IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsquamous</td>
<td>IHC 0</td>
</tr>
<tr>
<td>Squamous</td>
<td>IHC 3</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td>IHC 0</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td>IHC 1</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td>IHC 0</td>
</tr>
<tr>
<td>Squamous</td>
<td>IHC 2</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td>IHC 3</td>
</tr>
<tr>
<td>Squamous</td>
<td>IHC 3</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td>IHC 3</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td>IHC 0</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td>IHC 3</td>
</tr>
<tr>
<td>Nonsquamous</td>
<td>IHC 1</td>
</tr>
</tbody>
</table>

Patient experiencing ongoing benefit per investigator.
Patients first dosed at 1-20 mg/kg by Oct 1, 2012; data cutoff Apr 30, 2013.

Soria et al, ECCO 2013
Anti-PDL1 Development: NSCLC

**FIR Study: Phase II Dx-positive advanced mNSCLC**

- **PDL1 positive NSCLC** → Anti-PDL1 1200 mg IV Q3 weeks
- **Ongoing**
- **Primary end-point:**
  - Overall Response Rate

**POPLAR Study: Phase II 2/3L mNSCLC**

- **Metastatic NSCLC (2/3L)** → Docetaxel 75 mg/m2 IV Q3 wk
  - **Ongoing**
  - **Primary end-point:**
    - Overall Survival

- **Metastatic NSCLC (2/3L)** → Anti-PDL1 1200 mg IV Q3 wk

**OAK Study: Phase III 2/3L mNSCLC**

- **Metastatic NSCLC (2/3L)** → Docetaxel 75 mg/m2 IV Q3 wk
  - **Expect FPI:** Q1 2014
  - **Primary end-point:**
    - Overall Survival

- **Metastatic NSCLC (2/3L)** → Anti-PDL1 1200 mg IV Q3 wk
Performance up-date

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Summary
Summary: Focus on innovation and growth

1. Strategic focus on innovation and driving Personalised Healthcare

2. Strong growth in Emerging Markets facilitated by tailored access models

3. Leading product pipeline providing value for the future
Doing now what patients need next