Turning innovation into patient benefit

Karl Mahler
Head of Investor Relations

London, December 2015
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1. pricing and product initiatives of competitors;
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

Innovation and efficiency

Improving the standard of care

Outlook
Q3 2015: Sales growth for fifth consecutive year

All growth rates at constant exchange rates (CER)
HY 2015: Strong underlying Group core operating profit & margin

CHFbn

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>CER=Constant Exchange Rates</td>
<td>8.3</td>
<td>8.6</td>
<td>9.5</td>
<td>9.4</td>
<td>9.2</td>
</tr>
</tbody>
</table>

% of sales

- 38.1%
- 38.5%
- 40.7%
- 41.0%
- 39.2% (+0.4%p excl. filgrastim*)

+2% at CER (+7%*)

CER=Constant Exchange Rates

* Excluding sale of filgrastim rights in 2014 at CER
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

Innovation and efficiency

Improving the standard of care

Outlook
Roche strategy: Focused on medically differentiated therapies

**Regulators:**
Optimised benefit / risk ratio

**Payors:**
Optimised benefit / cost ratio
Roche/Genentech: Sustained record of cutting edge scientific discoveries

Research Publications in Cell, Science, or Nature

(* through Oct. 2015)
Roche’s strategy remains unchanged
*Success hinges on excellence in innovation & execution*

- Focus investment on **differentiated molecules**
- Continuously **improve processes**
Diversified approach towards innovation

**Belief: Exploring broad BUT prioritizing rigorously**

We invest more than others in the early stage

<table>
<thead>
<tr>
<th>% of budget dedicated R&amp;D phases</th>
<th>Industry avg</th>
<th>Roche</th>
</tr>
</thead>
<tbody>
<tr>
<td>R &amp; Early D</td>
<td>54%</td>
<td>60%</td>
</tr>
<tr>
<td>Late D</td>
<td>46%</td>
<td>40%</td>
</tr>
</tbody>
</table>

Research engines identified a growing n° of diverse solutions to patients’ needs

<table>
<thead>
<tr>
<th># of NME’s entering Pre-clinical</th>
<th>Genentech &amp; Roche &amp; CHUGAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>11</td>
</tr>
<tr>
<td>2012</td>
<td>18</td>
</tr>
<tr>
<td>2013</td>
<td>19</td>
</tr>
</tbody>
</table>

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.
However, we set a high bar for our R&D pipeline …

**Targeting clear differentiation in areas of unmet need**

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**Assessment for late stage entry candidates & line extensions**

<table>
<thead>
<tr>
<th>Unmet medical need</th>
<th>Clinical differentiation</th>
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<tbody>
<tr>
<td>low</td>
<td>low</td>
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<tr>
<td>high</td>
<td>high</td>
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</table>

**Threshold**

**Illustrative**

**Greater differentiation**

**Total sales potential**

- Continued
- Disqualified

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**Time**

**Sales**

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12
Roche’s strategy remains unchanged

*Success hinges on excellence in innovation & execution*

- Focus investment on *differentiated molecules*
- Continuously *improve processes*
We are also driving operational efficiencies

Select examples R&D

**Lean Protocol Design**
Rethinking protocol design to reduce complexity

**Sourcing Strategy**
Outsourcing transactional clinical operations roles

**Partnerships**
Industry consortium (20 companies) to drive trial efficiency

**All programs implementing lean protocols**


Other topics: Risk based monitoring, industry wide registries, etc.

Resulting in ~100m per year in savings
We are also driving operational efficiencies

Select examples Technical Operations

**Network efficiencies**

- Improve capacity planning across the network & align to future needs

**Complexity reduction**

- Remove >40% of all presentations by streamlining the EP\(^1\) portfolio (<0.1% sales impact\(^2\))

**Continuous process improvement**

- Implement lean principles, e.g. to decrease end-to-end cycle time by up to 50%\(^3\)

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**Optimize utilization & increase reliability**

**Focus resources on key value driver**

**Do the same with less**

Source: 1. Established Products  2. In 2016  3. For processes in scope
Achievements: Innovation

*Above-average R&D success rate*

Despite some set-backs, Roche continues to stay ahead of the industry

Note: Success rates calculated at the project/indication level for overlapping 5-year periods (9 data points between 2002-14) based on KMR data (with 13 Industry peers and Roche). From 2009 all Genentech projects are included; before that only those opted-in by Roche.
Achievements: Productivity

Doubled number of projects at same costs

Late stage development costs & number of projects

Excludes Chugai, pRED and gRED, Medical Affairs and PTD
Source: Roche internal development data
Performance update

Innovation and efficiency

Improving the standard of care

Outlook
New growth opportunities outside oncology

NMEs

<table>
<thead>
<tr>
<th>Year</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>Post 2017</th>
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<tr>
<td>alectinib</td>
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<tr>
<td></td>
<td>Herceptin + Perjeta</td>
<td>atezolizumab + chemo</td>
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<td></td>
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line extensions

- Oncology/hematology
- Neuroscience
- Ophthalmology
- Immunology

19
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
### Atezolizumab: Pivotal programs by disease

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

<table>
<thead>
<tr>
<th>Lung</th>
<th>Bladder</th>
<th>Kidney</th>
<th>Breast</th>
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</thead>
<tbody>
<tr>
<td>FIR and BIRCH</td>
<td>IMpower 130&amp;150</td>
<td>IMvigor 210</td>
<td>IMpassion 131</td>
</tr>
<tr>
<td>Dx+ mono</td>
<td>1L non-sq. combo</td>
<td>1L cis-inel. &amp; 2L</td>
<td>1L combo</td>
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<tr>
<td>POPLAR</td>
<td>IMpower 111</td>
<td>IMvigor 211</td>
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<tr>
<td>2L+ mono</td>
<td>1L sq. Dx+ mono</td>
<td>2L mono</td>
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<tr>
<td>OAK</td>
<td>IMpower 131</td>
<td>IMvigor 010</td>
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</tr>
<tr>
<td>2L mono</td>
<td>1L sq. combo</td>
<td>Adj.</td>
<td></td>
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<tr>
<td>IMpower 110</td>
<td>IMpower 010</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1L non-sq. Dx+ mono</td>
<td>Adj. Dx+ mono</td>
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- **cis-inel.** = cisplatin ineligible patients
- **Rolling filing initiated**
- **Phase 2**
- **Phase 3**
- **Data in 2016**
- **Data in 2017**

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21
### New growth opportunities outside oncology

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<td>Herceptin + Perjeta</td>
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<td>atezolizumab</td>
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#### Applications
- Oncology/hematology
- Neuroscience
- Ophthalmology
- Immunology
Three major types of Multiple Sclerosis

- **Relapse-Remitting (RRMS)** (60-65%)
  - Clearly defined relapses (attacks) with remissions initially returning to baseline but gradually result in sustained disability

- **Secondary Progressive (SPMS)** (20-25%)
  - Initial RRMS followed by disability accumulation. Still experience relapses which eventually stop

- **Primary Progressive (PPMS)** (10-15%)
  - Slow but nearly continuous worsening of disease from outset (no relapses)

- High unmet need:
  - high efficacy therapies have major safety issues
  - diagnosis and classification is difficult, often retrospective and can take 2-5 years

- Treatment decisions concentrated mainly in MS centers/hospitals

- Advocacy groups powerful in access

Adapted from Lublin 1996, Arnold 2004
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

Global sales (lc) USDm
New growth opportunities outside oncology

- alectinib
- ocrelizumab
- ACE910
- crenezumab
- taselisib
- etrolizumab
- Cotellic
- atezolizumab
- lampalizumab
- olesoxime
- venetoclax
- lebrikizumab
- etrolizumab
- 2015
- 2016
- 2017
- Post 2017
- Gazyva
- Gazyva
- Herceptin + Perjeta
- atezolizumab + chemo
- New growth opportunities outside oncology
- Oncology/hematology
- Neuroscience
- Ophthalmology
- Immunology
Hemophilia A: Current treatment strategies

**Episodic (on demand) treatment**
- Patients treated only when they bleed
- Can be up to 30-60 times per year

**Prophylaxis**
- Goal is to prevent bleeds
- IV infusion 2-3 times per week
- Can reduce bleed rate to 0-2 per year for non-inhibitor patients
- Should be the standard, but is still not used in ~35% of patients (treatment burden, adherence, IV access issues)
Hemophilia A: There are significant limitations of current treatment options

**FVIII market (USD 6.1bn in 2012)**

- **Current FVIII treatments**
  - Limited half-life of only 8-12 hrs
  - Frequent IV injections
  - Induce neutralizing antibodies, which inhibit their function

**By-passing agent market (USD 2.1bn)**

- **Current bypassing treatments**
  - Much shorter half-life of ~4-6 hrs
  - Multiple frequent IV infusions
  - Long infusion times (30+mins) for FEIBA
  - Unstable efficacy compared to FVIII

*Company reported sales; \(^1\)EvaluatePharma consensus analyst estimates
ACE910 can address the major medical needs for both inhibitor and non-inhibitor patients.

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

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

**Inhibitor**
- **Immune Tolerance Induction**
  - 70-80% success rate
  - limitation due to very high cost and heavy burden for patients
- **On-demand treatment with by-passing agents**
  - 2-3h intervals, IV
- **Prophylaxis with by-passing agents**
  - Every other day, IV

ACE 910

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

Maximising existing franchises

New growth opportunities

Biosimilars

Outlook
Current biosimilar trends
So far, sales have not achieved initial expectations

MAT 870 CHFm (June 2015)
(CAGR 25.5%)

*Excludes US as no biosimilars have been approved in the US so far (Omnitrope was approved under the 505(b) pathway)
IMS Health; MAT=moving annual total
Generics vs biosimilars
Clear divide in uptake; complex market drivers

Market share

Driven by price and patient offering
9 innovators, one biosimilar
Efficacy visible only longer term
No switching

Payer driven: 7 biosimilars
Efficacy visible immediately
High turnover of patients

Small molecule
Virtually disappear

Sources: IMS Biosimilar Dashboard, IMS & Roche analysis
1 Volume market share based on EU5 average;
2 Volume market share based on average of France & Germany EPO;
3 Data based on % remaining sales in EU
Despite 10 years of experience in the EU, uptake of biosimilars differs across countries

Reference: Assessing biosimilar uptake and competition in European markets. Report by the IMS Institute for Healthcare Informatics. HGH=human growth hormone; EPO=Erythropoietin; G-CSF=Granulocyte-colony stimulating factor
Performance up-date

Maximising existing franchises

New growth opportunities

Biosimilars

Outlook
Multiple major pivotal trials reading out near term
Significant filing and launch activities ahead

<table>
<thead>
<tr>
<th>Year</th>
<th>Molecule</th>
<th>Indication</th>
<th>Market opportunity</th>
<th>Incremental infrastructure</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>Alectinib</td>
<td>ALK+ NSCLC</td>
<td>Medium</td>
<td>Low to medium</td>
</tr>
<tr>
<td></td>
<td>Cotellic/Zelboraf</td>
<td>Melanoma</td>
<td>Medium</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Venetoclax</td>
<td>Hematology (CLL 17p del)*</td>
<td>Medium</td>
<td>Low</td>
</tr>
<tr>
<td>2016</td>
<td>Ocrelizumab</td>
<td>Multiple Sclerosis</td>
<td>Medium</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab</td>
<td>NSCLC, bladder (2/3L)</td>
<td>Medium</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Lebrikizumab</td>
<td>Asthma, AD, IPF, COPD</td>
<td>Large</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>APHINITY</td>
<td>Adj HER2+ breast cancer</td>
<td>Low</td>
<td></td>
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<tr>
<td></td>
<td>GOYA</td>
<td>NHL (aggressive)</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>ACE 910</td>
<td>Hemophilia A</td>
<td>Medium</td>
<td>Low to medium</td>
</tr>
<tr>
<td></td>
<td>Lampalizumab</td>
<td>Geographic atrophy</td>
<td>Low to medium</td>
<td>Low</td>
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<tr>
<td></td>
<td>GALLIUM</td>
<td>NHL (indolent)</td>
<td>Low</td>
<td></td>
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<tr>
<td></td>
<td>Atezolizumab+chemo</td>
<td>NSCLC (1L)</td>
<td>Low</td>
<td></td>
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<tr>
<td>2018</td>
<td>Taselisib (PI3Ki)</td>
<td>HER2-/HR+ breast cancer</td>
<td>Low to medium</td>
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<tr>
<td></td>
<td>Idasanutlin (MDM2)</td>
<td>Acute myeloid leukemia</td>
<td>Low to medium</td>
<td></td>
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</tbody>
</table>

Oncology  | Neuroscience  | Ophthalmology  | Immunology
Small: up to CHF 0.5 bn | medium= CHF 0.5 to CHF 1bn | large > CHF1bn

NSCLC=non-small cell lung cancer; CLL=chronic lymphocytic leukemia; AD=atopic dermatitis; IPF=idiopathic pulmonary fibrosis; COPD=chronic obstructive pulmonary disease; NHL=non-hodgkin’s lymphoma; * first indication
Positive outlook

Strong pipeline mitigates biosimilar impact

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

Biosimilars
MabThera, Herceptin, Avastin
### Planned key data presentations in H2 2015

<table>
<thead>
<tr>
<th>Event</th>
<th>Dates</th>
<th>Location</th>
<th>Presentations</th>
</tr>
</thead>
</table>
| 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  
- PPMS: ORATORIO 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) |

\(^1\) “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

<table>
<thead>
<tr>
<th>Category</th>
<th>Forecast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group sales growth(^1)</td>
<td>Low to mid-single digit</td>
</tr>
<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>
</tbody>
</table>

\(^1\) At constant exchange rates  
\(^2\) Excluding sale of filgrastim rights in 2014
Range of treatment options in RMS
Varying efficacy and safety profiles

ILLUSTRATIVE

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Safety/Use</th>
</tr>
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<tbody>
<tr>
<td>More</td>
<td>More / Earlier</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>Natalizumab (JCV+)</td>
</tr>
<tr>
<td>Natalizumab (JCV-)</td>
<td>Fingolimod</td>
</tr>
<tr>
<td>Dimethyl fumarate</td>
<td>ABCRs (Interferons and Copaxon)</td>
</tr>
<tr>
<td>Teriflunomide</td>
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<tr>
<td>Less / Later</td>
<td>Less</td>
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</tbody>
</table>

Unmet need

RMS=relapsing forms of multiple sclerosis; ABCR=Avonex®; Betaseron®; Copaxon®; Rebif®;
## New growth opportunities outside oncology

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### Line extensions
- Oncology/hematology
- Neuroscience
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- Immunology
Severe asthma: High unmet need in growing market

Global asthma market 2014 vs 2020

- Approx. 300m patients worldwide and growing strongly
- 5-10% asthma patients have severe disease, and ~30% of severe disease is uncontrolled despite maximal therapy
- Over 4.5m severe asthmatics with uncontrolled disease

Note: Market shares based on value (sales); Source: Evaluate; defined by daily use of ≥500ug ICS + LABA
Asthma: Biologic market expected to grow strongly to CHF 5bn by 2020

New guidelines

New biologics with different MoAs within 5yrs

Biomarkers: Emergence of phenotyping

1. Decision resources, Asthma (Moderate to Severe), April 2014. Timeframe considered = when mepolizumab, reslizumab and lebrikizumab will be available; 2. Evaluate pharma, analysis on January 28th 2015; OCS=oral corticosteroid; MoA=mechanism of action
Doing now what patients need next