Innovation and value creation

Alan Hippe, CFO Roche Group

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6. increased government pricing pressures;
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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

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<thead>
<tr>
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<tbody>
<tr>
<td>Amount</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

- HY 2011: 38'1%
- HY 2012: 38'5%
- HY 2013: 40'7%
- HY 2014: 41'0%
- HY 2015: 39'2% (+0.4%p excl. filgrastim*)

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

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Outlook
Roche strategy: Focused on medically differentiated therapies

Regulators:
Optimised benefit / risk ratio

Payors:
Optimised benefit / cost ratio
Roche’s strategy remains unchanged
Success hinges on excellence in innovation & execution

✔️ Focus investment on differentiated molecules

☐ Continuously improve processes
Roche/Genentech: Sustained record of cutting edge scientific discoveries

Research publications in Cell, Science, or Nature

(* through Oct. 2015)
Approach towards innovation
Exploring broad …

We invest more early stage

% of budget

R & Early D
54%
60%

Late D
46%
40%

Industry avg
Roche

…to increase options to choose from

# of NME’s entering Pre-clinical

2012
2013
2014

Industry avg.

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

Clinical differentiation

Threshold

Sales

Greater differentiation

Time

Continued

Disqualified
Achievements: Innovation

Above-average R&D success rate

Likelihood of launch from phase 0

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
Roche’s strategy remains unchanged

*Success hinges on excellence in innovation & execution*

- Focus investment on **differentiated molecules**
- Continuously **improve processes**
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

Savings of ~100m CHF per year
Driving operational efficiencies
Optimization production capacities

Highly potent small molecules with lower capacity requirements

Pipeline of large molecules and entry into new high volume segments

Savings of ~100m CHF per year
Performance update

Innovation and efficiency

Improving the standard of care

Outlook
New growth opportunities outside oncology

<table>
<thead>
<tr>
<th>Year</th>
<th>NMEs</th>
<th>Line Extensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>alectinib, venetoclax</td>
<td>Herceptin + Perjeta</td>
</tr>
<tr>
<td>2016</td>
<td>ocrelizumab, lebrikizumab</td>
<td>Gazyva</td>
</tr>
<tr>
<td>2017</td>
<td>ACE910, atezolizumab</td>
<td>atezolizumab + chemo, Gazyva</td>
</tr>
<tr>
<td>Post 2017</td>
<td>gantenerumab, crenezumab, taselisib, lampalizumab, olesoxime, etrolizumab</td>
<td></td>
</tr>
</tbody>
</table>

**Areas of interest:**
- Oncology/hematology
- Neuroscieence
- Ophthalmology
- Immunology
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

<table>
<thead>
<tr>
<th>Lung</th>
<th>Bladder</th>
<th>Kidney</th>
<th>Breast</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIR and BIRCH</td>
<td>IMpower 130 &amp; 150</td>
<td>IMvigor 210</td>
<td>IMmotion 150</td>
</tr>
<tr>
<td>Dx+ mono</td>
<td>1L non-sq. combo</td>
<td>1L cis-inel. &amp; 2L</td>
<td>1L combo</td>
</tr>
<tr>
<td>POPLAR</td>
<td>IMpower 111</td>
<td>IMvigor 211</td>
<td>IMmotion 151</td>
</tr>
<tr>
<td>2L+ mono</td>
<td>1L sq. Dx+ mono</td>
<td>2L mono</td>
<td>1L combo</td>
</tr>
<tr>
<td>OAK</td>
<td>IMpower 131</td>
<td>IMvigor 010</td>
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<tr>
<td>2L mono</td>
<td>1L sq. combo</td>
<td>Adj.</td>
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<tr>
<td>IMpower 110</td>
<td>IMpower 010</td>
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<tr>
<td>1L non-sq. Dx+ mono</td>
<td>Adj. Dx+ mono</td>
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</tbody>
</table>

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

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

cis-inel. = cisplatin ineligible patients
### New growth opportunities outside oncology

<table>
<thead>
<tr>
<th>NMEs</th>
<th>Post 2017</th>
<th>2017</th>
<th>2016</th>
<th>2015</th>
</tr>
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<tbody>
<tr>
<td>alectinib</td>
<td>gantenerumab</td>
<td>ACE910</td>
<td>ocrelizumab</td>
<td>alectinib</td>
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<tr>
<td>Cotellic</td>
<td>crenezumab</td>
<td>atezolizumab</td>
<td>lebrikizumab</td>
<td>Cotellic</td>
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<tr>
<td>venetoclax</td>
<td>taselisib</td>
<td>lampalizumab</td>
<td>olesoxime</td>
<td>venetoclax</td>
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<tr>
<td></td>
<td>etrolizumab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herceptin + Perjeta</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Gazyva</td>
<td></td>
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<tr>
<td>2016</td>
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<td></td>
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<tr>
<td>2017</td>
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<tr>
<td>Gazyva</td>
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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

- Betaseron
- Rebif
- Avonex
- Copaxone
- ABCRs
- New biologics
- Orals
- Lemtrada
- Tysabri
- Tecfidera
- Aubagio
- Gilenya*
New growth opportunities outside oncology

<table>
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<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>Post 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>alectinib</td>
<td>Herceptin + Perjeta</td>
<td>atezolizumab + chemo</td>
<td>Gazyva</td>
<td></td>
</tr>
<tr>
<td>Cotellic</td>
<td>ocrelizumab</td>
<td>lampalizumab</td>
<td>Gazyva</td>
<td></td>
</tr>
<tr>
<td>venetoclax</td>
<td>lebrikizumab</td>
<td>olesoxime</td>
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- Oncology/hematology
- Neuroscience
- Ophthalmology
- 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
Lebrikizumab in severe uncontrolled asthma

High efficacy and improved convenience

**Summary phase II results:**

- Exacerbation reduction of 60%
- Early onset of lung function improvement (FEV1)
- Prefilled syringe and Q4W subcutaneous delivery for improved convenience
Performance update

Innovation and efficiency

Improving the standard of care

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>Low to medium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cotetlic/Zelboraf</td>
<td>Melanoma</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Venetoclax</td>
<td>Hematology (CLL 17p del)*</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>Ocrelizumab</td>
<td>Multiple Scelerosis</td>
<td>Medium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atezolizumab</td>
<td>NSCLC, bladder (2/3L)</td>
<td>Medium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lebrikizumab</td>
<td>Asthma, AD, IPF, COPD</td>
<td>Large</td>
<td></td>
</tr>
<tr>
<td></td>
<td>APHINITY</td>
<td>Adj HER2+ breast cancer</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GOYA</td>
<td>NHL (aggressive)</td>
<td>Low</td>
<td></td>
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<tr>
<td>2017</td>
<td>ACE 910</td>
<td>Hemophilia A</td>
<td>Low to medium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lampalizumab</td>
<td>Geographic atrophy</td>
<td>Low to medium</td>
<td></td>
</tr>
<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 (PI3Kι)</td>
<td>HER2-/HR+ breast cancer</td>
<td>Low to medium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Idasanutlin (MDM2)</td>
<td>Acute myeloid leukemia</td>
<td>Low to medium</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Small: up to CHF 0.5 bn</th>
<th>Medium: CHF 0.5 to CHF 1bn</th>
<th>Large: &gt; CHF1bn</th>
</tr>
</thead>
</table>

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, Cotellie, Ocrelizumab, Atezolizumab, Lebrikizumab, ACE910, Lampalizumab

Biosimilars
MabThera, Herceptin, Avastin

Marketed products

Pipeline

Conceptual

Sales

## 2015 outlook: Guidance upgraded

<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group sales growth(^1)</td>
<td>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 (CER)
2 Excluding sale of filgrastim rights in 2014
New growth opportunities outside oncology

- alectinib
- ocrelizumab
- ATE910
- Gantenerumab

- Cotellic
- Atezolizumab
- Lampalizumab
- Crenezumab

- Venetoclax
- Lebrikizumab
- Olesoxime
- Etrolizumab

- Venetoclax + Ocolizumab + Chemo
- Gazyva
- Gazyva
- Gazyva

- Herceptin + Perjeta
- Gazyva
- Gazyva

- 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; ¹EvaluatePharma consensus analyst estimates
ACE910 can address the major medical needs for both inhibitor and non-inhibitor patients

## Non-Inhibitor

<table>
<thead>
<tr>
<th>On-demand treatment</th>
<th>Prophylaxis treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3 times/bleeding event, IV</td>
<td>3 times/week, IV</td>
</tr>
</tbody>
</table>

### 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
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
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
Doing now what **patients** need next