Innovation and value creation

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Performance update

Innovation and efficiency

Improving the standard of care

Outlook
Q1 2016: Sales growth for fifth consecutive year

All growth rates at Constant Exchange Rates (CER)
Q1 2016: Solid sales growth in all regions

CHFbn

Japan: +4% (Diagnostics), -3% (Pharma)
International: +16% (Diagnostics), +4% (Pharma)
Europe: -1% (Diagnostics), +5% (Pharma)
US: 0% (Diagnostics), +3% (Pharma)

All growth rates at Constant Exchange Rates (CER)
Roche significantly advancing patient care
Recognition for innovation 2013-present

### Breakthrough Therapy Designations

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>#</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Roche</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>BMS</td>
<td>8</td>
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<tr>
<td>3</td>
<td>Novartis</td>
<td>7</td>
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<td>3</td>
<td>Merck</td>
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<td>3</td>
<td>Pfizer</td>
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<td>4</td>
<td>GSK</td>
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<table>
<thead>
<tr>
<th>Year</th>
<th>Molecule</th>
</tr>
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<tbody>
<tr>
<td>2016</td>
<td><strong>Ocrelizumab</strong> <em>(PPMS)</em></td>
</tr>
<tr>
<td></td>
<td><strong>Venclexta</strong> <em>(AML)</em></td>
</tr>
<tr>
<td></td>
<td><strong>Venclexta + Rituxan</strong> <em>(R/R CLL)</em></td>
</tr>
<tr>
<td>2015</td>
<td><strong>Actemra</strong> <em>(Systemic sclerosis)</em></td>
</tr>
<tr>
<td></td>
<td><strong>Atezolizumab</strong> <em>(NSCLC)</em></td>
</tr>
<tr>
<td></td>
<td><strong>Venclexta</strong> <em>(R/R CLL 17p del)</em></td>
</tr>
<tr>
<td></td>
<td><strong>Emicizumab</strong>/<em>ACE 910</em>* <em>(Hemophilia A)</em></td>
</tr>
<tr>
<td>2014</td>
<td><strong>Esbriet</strong> <em>(IPF)</em></td>
</tr>
<tr>
<td></td>
<td><strong>Lucentis</strong> <em>(DR)</em></td>
</tr>
<tr>
<td></td>
<td><strong>Atezolizumab</strong> <em>(Bladder)</em></td>
</tr>
<tr>
<td>2013</td>
<td><strong>Alectinib</strong> <em>(2L ALK+ NSCLC)</em></td>
</tr>
<tr>
<td></td>
<td><strong>Gazyva</strong> <em>(1L CLL)</em></td>
</tr>
</tbody>
</table>

Source: [http://www.focr.org/breakthrough-therapies](http://www.focr.org/breakthrough-therapies) as at 22 March 2016; PPMS=Primary Progressive Multiple Sclerosis; CLL=Chronic Lymphocytic Leukemia; NSCLC=Non-Small Cell Lung Cancer; IPF=Idiopathic Pulmonary Hypertension; DR=Diabetic Retinopathy
2015: Strong underlying Group Core operating profit & margin

CER=Constant Exchange Rates; * Excluding sale of filgrastim rights in 2014
2015: Dividend and payout ratio further increased

Payout ratio calculated as dividend per share divided by Core earnings per share (diluted); 2015 dividend as proposed by the Board of Directors; 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’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…to increase options to choose from

% of budget

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

# of NME’s entering Pre-clinical

<table>
<thead>
<tr>
<th></th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Industry avg.</td>
<td>11</td>
<td>18</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.
Approach towards innovation

…but prioritizing rigorously

We select at late stage entry

Illustrative

Medical need

low

high

low

Clinical differentiation

high

Threshold

...to increase sales potential

Sales

Greater differentiation

Continued

Disqualified

Time
Achievements: Innovation

Above-average R&D success rate

Note: Success rates calculated at the project/indication level for overlapping 5-year periods based on KMR data (13 peers and Roche)
Strengthening Pharma through collaborations
Data analysis driving innovation and efficiencies

Access meaningful data

Diagnostic Data
Clinical Trial Data
Real World Data

Create insights
Advanced analytics of integrated data

Realise value
Smarter, more efficient R&D
Improved access & personalised patient care
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

Small molecules

- Highly potent small molecules with lower capacity requirements

Large molecules

- 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

- alectinib
- ocrelizumab
- ACE910
- gantenerumab
- crenezumab
- taselisib
- lampalizumab
- etrolizumab
- lebrikizumab
- olesoxime
- etrolizumab
- venetoclax
- atezolizumab
- lebrikizumab
- gantenerumab

**Year**
- 2015: 
  - Herceptin + Perjeta
  - Gazyva
- 2016: 
  - Herceptin + Perjeta
  - Gazyva
- 2017: 
  - Herceptin + Perjeta
  - Gazyva
- Post 2017: 
  - Herceptin + Perjeta
  - Gazyva

**Categories**
- Oncology/hematology
- Neuroscience
- Ophthalmology
- Immunology
New growth opportunities

NMEs

- alectinib
- Cotellic
- venetoclax
- ocrelizumab
- lebrikizumab
- atezolizumab
- ACE910
- lampalizumab
- olesoxime
- gantenerumab
- crenezumab
- taselisib
- etrolizumab

Line extensions

- 2015
- 2016
- 2017
- Post 2017

- Herceptin + Perjeta
- Gazyva
- atezolizumab + chemo
- Gazyva

Oncology/hematology
Neuroscience
Ophthalmology
Immunology
10 novel own CIT assets in clinical development

Targeting cancer through different mechanisms

**Priming & activation**
- anti-CEA-IL2v FP (cergutuzumab)
- anti-FAP-IL2v FP
- anti-OX40

**Antigen presentation**
- anti-CD40

**Antigen release**

**T cell trafficking**

**T cell infiltration**
- anti-Ang2/VEGF (vanucizumab)

**Cancer T cell recognition**
- anti-CEA/CD3 TCB
- anti-CD20/CD3 TCB

**T cell killing**
- anti-PDL1 (atezolizumab)
- anti-CSF-1R (emactuzumab)
- IDOi (NewLink)

Chen and Mellman. Immunity 2013

NME=new molecular entity; CIT=cancer immunotherapy; FP=fusion protein; TCB=T-cell bispecific
Combination trials as of beginning 2015…

- **Launched/late-stage portfolio**
- **Chemotherapy combinations approved**
- **Targeted combinations approved**
- **Roche combinations in trials**
- **Chemotherapy combinations in trials**

**NMEs late stage**
- **NMEs early stage**

- **aCSF**
- **1R**
- **aCEA**
- **IL2v FP**
- **aOX40**
- **aCD40**
- **IDO**
- **aCEA/CD3 TCB**

- **atezolizumab**
- **cobimetinib**
- **venetoclax**
- **polatuzumab**
- **alectinib**

- **Launched late-stage portfolio**
- **Immunotherapy portfolio**

- **Roche**
Combination therapies now
Maximising our unique oncology portfolio
New growth opportunities outside oncology

- alectinib
- Cotellic
- venetoclax
- ocrelizumab
- atezolizumab
- lebrikizumab
- ACE910
- lampalizumab
- olesoxime
- etrolizumab
- gantenerumab
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- 2015
- 2016
- 2017
- Post 2017

- Herceptin + Perjeta
- Gazyva
- atezolizumab + chemo
- Gazyva

- Oncology/hematology
- Neuroscience
- Ophthalmology
- Immunology
Ocrelizumab: Active in both RRMS & PPMS

- Selective depletion of a B cell subset leaving the ability to generate new B cells intact
- Administered IV twice yearly

Time to 12-week CDP

Time to 24-week CDP

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;
Secondary Endpoints: Significant reduction in number of T1 Gd+ lesions compared with IFN β-1a

**Safety summary**
Overall, in OPERA I and OPERA II, ocrelizumab had a similar safety profile compared with IFN β -1a over 96 weeks.

*ITT*
*Adjusted by means calculated by negative binomial regression and adjusted for baseline T1 Gd lesion (present or not), baseline EDSS (<4.0 vs ≥4.0) and geographical region (US vs ROW).
EDSS, Expanded Disability Status Scale; Gd+, gadolinium enhancing; IFN, interferon; MRI, magnetic resonance imaging; ROW, rest of the world.
Multiple Sclerosis: Improvements over SoC driving market growth

Global sales (lc) USDm

Source: Evaluate Pharma Multiple Sclerosis report, October 2015; * Includes Imusera sales; SoC=standard of care
New growth opportunities outside oncology

### NMEs

**2015**
- alectinib
- Cotellic
- venetoclax

**2016**
- ocrelizumab
- lebrikizumab

**2017**
- ACE910
- atezolizumab

**Post 2017**
- gantenerumab
- crenezumab
- taselisib
- lampalizumab
- etrolizumab
- olesoxime

### Line extensions

**2015**
- Herceptin + Perjeta
- Gazyva

**2016**
- Gazyva

**2017**
- atezolizumab + chemo

**Post 2017**
- Gazyva

- **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)
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

**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

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**ACE 910**

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

Innovation and efficiency

Improving the standard of care

Outlook
### Significant launch activities ahead

#### Pharma

<table>
<thead>
<tr>
<th>Year</th>
<th>Drug</th>
<th>Disease Area</th>
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<tbody>
<tr>
<td>2016</td>
<td>Venclextra</td>
<td>R/R CLL with 17p del</td>
</tr>
<tr>
<td></td>
<td>Cotelllic + Zelboraf</td>
<td>BRAFmut melanoma</td>
</tr>
<tr>
<td></td>
<td>Alecensa</td>
<td>2L ALK+ NSCLC</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab</td>
<td>2L+ lung and bladder cancer</td>
</tr>
<tr>
<td></td>
<td>Gazyva</td>
<td>Refractory iNHL (GADOLIN)</td>
</tr>
<tr>
<td>2017</td>
<td>Emicizumab (ACE910)</td>
<td>Hemophilia A</td>
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<tr>
<td></td>
<td>Lebrikizumab</td>
<td>Severe Asthma</td>
</tr>
<tr>
<td></td>
<td>Ocrelizumab</td>
<td>RMS/ PPMS</td>
</tr>
<tr>
<td></td>
<td>Perjeta + Herceptin</td>
<td>eBC HER2+ (APHINITY)</td>
</tr>
<tr>
<td></td>
<td>Gazyva</td>
<td>1L aNHL (GOYA)</td>
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<tr>
<td></td>
<td>Actemra</td>
<td>Giant cell arteritis</td>
</tr>
<tr>
<td>2018</td>
<td>Lampalizumab</td>
<td>Geographic atrophy</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab + Avastin + chemo</td>
<td>1L NSCLC</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab + Avastin</td>
<td>1L RCC</td>
</tr>
<tr>
<td></td>
<td>Gazyva</td>
<td>1L iNHL (GALLIUM)</td>
</tr>
<tr>
<td></td>
<td>Alecensa</td>
<td>1L ALK+ NSCLC</td>
</tr>
</tbody>
</table>

#### Diagnostics

| 2016 | cobas e 801 launch in immunodiagnostics |
| 2017 | cobas t 511 cobas t 711 |
| 2018 | cobas 6000 (new) |

### Outcome studies are event-driven: timelines may change. Standard approval timelines of 1 year assumed.
Positive outlook

Strong pipeline mitigates biosimilar impact

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

Biosimilars
MabThera, Herceptin, Avastin
## 2016 outlook

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<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</td>
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<tr>
<td>Dividend outlook</td>
<td>Further increase dividend in Swiss francs</td>
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</tbody>
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\(^1\) At Constant Exchange Rates (CER)
Appendix
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>
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<tbody>
<tr>
<td>2015</td>
<td>Alectinib</td>
<td>ALK+ NSCLC</td>
<td>⬤⬤⬤</td>
<td>Low to medium</td>
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<td></td>
<td>Cotelic/Zelboraf</td>
<td>Melanoma</td>
<td>⬤⬤⬤</td>
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<td></td>
<td>Venetoclax</td>
<td>Hematology (CLL 17p del)*</td>
<td>⬤⬤⬤</td>
<td>Low</td>
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<tr>
<td>2016</td>
<td>Ocrelizumab</td>
<td>Multiple Sclerosis</td>
<td>⬤⬤⬤</td>
<td>Medium</td>
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<tr>
<td></td>
<td>Atezolizumab</td>
<td>NSCLC, bladder (2/3L)</td>
<td>⬤⬤⬤</td>
<td>Medium</td>
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<tr>
<td></td>
<td>Lebrikizumab</td>
<td>Asthma, AD, IPF, COPD</td>
<td>⬤⬤⬤</td>
<td>Large</td>
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<tr>
<td></td>
<td>APHINITY</td>
<td>Adj HER2+ breast cancer</td>
<td>⬤⬤⬤</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>GOYA</td>
<td>NHL (aggressive)</td>
<td>⬤⬤⬤</td>
<td>Low</td>
</tr>
<tr>
<td>2017</td>
<td>ACE 910</td>
<td>Hemophilia A</td>
<td>⬤⬤⬤</td>
<td>Low to medium</td>
</tr>
<tr>
<td></td>
<td>Lampalizumab</td>
<td>Geographic atrophy</td>
<td>⬤⬤⬤</td>
<td>Low to medium</td>
</tr>
<tr>
<td></td>
<td>GALLIUM</td>
<td>NHL (indolent)</td>
<td>⬤⬤⬤</td>
<td>Low</td>
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<tr>
<td></td>
<td>Atezolizumab+chemo</td>
<td>NSCLC (1L)</td>
<td>⬤⬤⬤</td>
<td>Low</td>
</tr>
<tr>
<td>2018</td>
<td>Taselisib (PI3Ki)</td>
<td>HER2-/HR+ breast cancer</td>
<td>⬤⬤⬤</td>
<td>Low to medium</td>
</tr>
<tr>
<td></td>
<td>Idasanutlin (MDM2)</td>
<td>Acute myeloid leukemia</td>
<td>⬤⬤⬤</td>
<td>Low to medium</td>
</tr>
</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
Three major types of Multiple Sclerosis

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

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

3. **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*
Doing now what patients need next
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
Ocrelizumab: Active in both RRMS & PPMS

Primary endpoint

Key secondary

Safety summary

Overall, in ORATORIO ocrelizumab had a favorable safety profile

Analysis based on ITT population; p-value based on log-rank test stratified by geographic region and age.

Patients with initial disability progression who discontinued treatment early with no confirmatory EDSS assessment were considered as having confirmed disability progression. CDP, confirmed disability progression; EDSS, Expanded Disability Status Scale; HR, hazard ratio; ITT, intent to treat.

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;