Innovation and value creation

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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;
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6. increased government pricing pressures;
7. interruptions in production;
8. loss of or inability to obtain adequate protection for intellectual property rights;
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Performance update

Innovation and efficiency

Improving the standard of care

Outlook
2015: Targets fully achieved

<table>
<thead>
<tr>
<th>Targets for 2015</th>
<th>FY 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group sales growth</strong>¹</td>
<td>Mid-single digit</td>
</tr>
<tr>
<td><strong>Core EPS growth</strong>¹</td>
<td>Ahead of sales growth²</td>
</tr>
<tr>
<td><strong>Dividend outlook</strong></td>
<td>Further increase dividend in Swiss francs³ (Payout ratio increased to 60% from 56%)</td>
</tr>
</tbody>
</table>

1 At constant exchange rates (CER); ² Excluding sale of filgrastim rights in 2014; ³ 2015 dividend as proposed by the Board of Directors
2015: Strong sales growth in all regions

All growth rates are YoY at Constant Exchange Rates (CER)
2015: Strong underlying Group Core operating profit & margin

<table>
<thead>
<tr>
<th>Year</th>
<th>CHFbn</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>15.1</td>
</tr>
<tr>
<td>2012</td>
<td>17.2</td>
</tr>
<tr>
<td>2013</td>
<td>17.9</td>
</tr>
<tr>
<td>2014</td>
<td>17.6</td>
</tr>
<tr>
<td>2015</td>
<td>17.5</td>
</tr>
</tbody>
</table>

% of sales

- 2011: 35.6%
- 2012: 37.7%
- 2013: 38.3%
- 2014: 37.2%
- 2015: 36.4% (+0.7%*)

+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

Graph showing differentiated therapies with Focus on Pharma and Dia, and other categories like Generics, OTC, MedTech at lower levels of differentiation.
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

<table>
<thead>
<tr>
<th>% of budget</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>
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</tbody>
</table>

# of NME’s entering Pre-clinical

<table>
<thead>
<tr>
<th>Year</th>
<th>Industry avg</th>
<th>Roche</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

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

Illustrative

Medical need

low

low

Clinical differentiation

low

high

Threshold

…to increase sales potential

Sales

Continued

Disqualified

Greater differentiation

Time
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)
Strengthening Pharma through collaborations

Data analysis driving innovation and efficiencies

Access meaningful data

Create insights

Realise value

Diagnostic Data

Clinical Trial Data

Real World Data

Advanced analytics of integrated data

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 outside oncology

- alectinib
- ocrelizumab
- ACE910
- gantenerumab
- crenezumab
- taselisib
- etrolizumab
- venetoclax
- lebrikizumab
- lampalizumab
- etrolizumab
- Cotellic
- atezolizumab
- olesoxime
- Herceptin + Perjeta
- Gazyva

- 2015
- 2016
- 2017
- Post 2017

- Oncology/hematology
- Neuroscience
- Ophthalmology
- Immunology
The 7 steps of the Cancer-Immunity Cycle guide our prioritization framework for Atezolizumab and our CI portfolio

1. Antigen presentation
   - T-Vect oncolytic viruses* (Amgen)
   - INFα
   - anti-CD40
   - CMB305 vaccine* (Immune Design)

2. Priming & activation
   - anti-CEA-IL2v FP
   - anti-OX40
   - anti-CD27* (CellGex)
   - entinostat* (Syndax)

3. T-cell Trafficking
   - blood vessel

4. T-cell infiltration
   - anti-VEGF (Avastin)
   - anti-Ang2/VEGF (vanucizumab)

5. Cancer T-cell recognition
   - anti-CEA/CD3 TCB
   - anti-CD20/CD3 TCB
   - anti-HER2/CD3 TCB
   - ImmTAC* (Immunocore)

6. Antigen release
   - EGFRi (Tarceva)
   - ALKi (Alectinib)
   - BRAFi (Zelboraf)
   - MEKi (Cotellic)
   - anti-CD20 (Gazyva)
   - anti-HER2 (Herceptin; Kadcyla; Perjeta)
   - various chemotherapies
   - lenalidomide*
   - rociletinib* (Clovis)

7. T-cell killing
   - anti-PDL1 (atezolizumab)
   - anti-CSF-1R (emactuzumab)
   - IDOi (NewLink)
   - IDOi* (Incyte)
   - CPI-444* (Corvus)
   - anti-TIGIT
   - IDO1/TDOI* (Curadev)

Chen and Mellman. Immunity 2013
Combination trials as of beginning 2015…

Launched/late-stage portfolio

Targeted combinations approved
Chemotherapy combinations approved
Roche combinations in trials
Chemotherapy combinations in trials
NMEs late stage
NMEs early stage
...and combination trials as of today
Cancer Immunology Research Focus: The Next Generation

- Cancer cell death and release of cancer proteins
- Initiation of Immune Response
- T cell activation and expansion
- Immune cell trafficking and infiltration
- Immune suppression

**Costimulators:**
- Anti-OX40 Ab (Ph 1)
- NME1

**Stromal modifiers:**
- NME2
- NME3

**Inhibitory checkpoints:**
- Anti-TIGIT Ab (ED)
- NME4
- NME5
- NME6

**T<sub>R</sub> cells:**
- Anti-OX40 Ab (Ph 1)
- IDO SMI (Ph 1)
- NME7
- NME8
anti-OX40: Dual Action Promotes T cell Activation and T Regulatory Cell Inhibition

anti-OX40: Promising Anti-Tumor Activity as Single Agent and in Combination with anti-PD-L1

Ongoing studies

- Phase 1a (MOXR0916)
- Phase 1b combination (MOXR0916 + atezolizumab)
- Planned (MOXR0916 + GDC-0919)
Cancer immunotherapy read-outs in 2016

### Phase I

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Tumors / Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>atezolizumab</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + chemo</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + Tarceva</td>
<td>NSCLC</td>
</tr>
<tr>
<td>atezolizumab + Zelboraf</td>
<td>Melanoma</td>
</tr>
<tr>
<td>atezolizumab + Cotelic</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + Gazyva</td>
<td>R/R FL/aNHL</td>
</tr>
<tr>
<td>atezolizumab + Avastin+/–chemo</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab + lenalidomide</td>
<td>MM</td>
</tr>
<tr>
<td>atezolizumab + Zelboraf + Cotelic</td>
<td>Melanoma</td>
</tr>
<tr>
<td>atezolizumab + Alecensa</td>
<td>ALK+ NSCLC</td>
</tr>
<tr>
<td>atezolizumab + /–azacitidine</td>
<td>MDS</td>
</tr>
<tr>
<td>atezolizumab + Gazyva + chemo</td>
<td>R/R FL/aNHL</td>
</tr>
<tr>
<td>atezolizumab + Gazyva + lenalidomide</td>
<td>R/R FL/aNHL</td>
</tr>
<tr>
<td>atezolizumab + Kadcyla/Herceptin+Perjeta</td>
<td>HER2+ eBC/mBC</td>
</tr>
<tr>
<td>atezolizumab + Gazyva + polatuzumab</td>
<td>R/R FL/aNHL</td>
</tr>
</tbody>
</table>

### Phase II

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Tumors / Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>atezolizumab</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aCD20/CD3 TCB</td>
<td>heme tumors</td>
</tr>
<tr>
<td>aCD20/CD3 TCB</td>
<td>heme tumors</td>
</tr>
<tr>
<td>aFAP-IL2v FP</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aFAP-IL2v FP</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aCD40</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aCD40</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aOX40</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aOX40</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aCEA-IL2v FP</td>
<td>Solid tumors</td>
</tr>
<tr>
<td>aCEA-IL2v FP</td>
<td>Solid tumors</td>
</tr>
</tbody>
</table>

### Phase III

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Tumors / Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>atezolizumab</td>
<td>2/3L NSCLC</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>2/3L NSCLC</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>1L non sq NSCLC</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>1L non sq NSCLC</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>1L sq NSCLC</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>1L sq NSCLC</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>1L non sq NSCLC (Dx+)</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>1L sq NSCLC (Dx+)</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>1L TNBC</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>1L Renal</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>Adjuvant MIBC (Dx+)</td>
</tr>
<tr>
<td>atezolizumab</td>
<td>Adjuvant NSCLC (Dx+)</td>
</tr>
</tbody>
</table>

### Notes
- atezolizumab trials
- NME monotherapy
- Immune doublets
- Results in 2016

Status as of Jan 28, 2016; Outcome studies are event-driven: timelines may change.
New growth opportunities outside oncology

- NMEs
  - alectinib
  - Cotellic
  - venetoclax
  - ocrelizumab
  - atezolizumab
  - lebrikizumab
  - Gazyva

- Line extensions
  - Herceptin + Perjeta
  - Ace910
  - Ocrelizumab
  - Atezolizumab + chemo
  - Gazyva

- Post 2017
  - Gantenerumab
  - Crenezumab
  - Taselisib
  - Lampalizumab
  - Olesoxime
  - Etrolizumab

- Fields
  - 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

**RRMS**

**Time to 12-week CDP**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Proportion of Patients Having CDP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN-β-1a 44 µg (n=829)</td>
<td>15.2</td>
</tr>
<tr>
<td>Ocrelizumab 600 mg (n=827)</td>
<td>9.8</td>
</tr>
</tbody>
</table>

Risk reduction: 40%
HR (95% CI): 0.60 (0.45, 0.81); p=0.00006

**Time to 24-week CDP**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Proportion of Patients Having CDP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN-β-1a 44 µg (n=829)</td>
<td>12.0</td>
</tr>
<tr>
<td>Ocrelizumab 600 mg (n=827)</td>
<td>7.6</td>
</tr>
</tbody>
</table>

Risk reduction: 40%
HR (95% CI): 0.60 (0.43, 0.84); p=0.0025

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

*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.
Ocrelizumab: Active in both **RRMS & PPMS**

**Primary endpoint**

**Key secondary**

### Time to 12-week Confirmed Disability Progression

- **Placebo (n=244)**
- **Ocrelizumab 600 mg (n=488)**

- **24% reduction in risk of CDP**
  - HR (95% CI): 0.76 (0.59, 0.98); *p*=0.0321

### Time to 24-week Confirmed Disability Progression

- **Placebo (n=244)**
- **Ocrelizumab 600 mg (n=488)**

- **25% reduction in risk of CDP**
  - HR (95% CI): 0.75 (0.58, 0.98); *p*=0.0365

---

**Safety summary**

Overall, in ORATORIO ocrelizumab had a favorable safety profile

---

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

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

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

line extensions

- 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

**ACE 910**

**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**

**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

**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
2016 onwards: Significant launch activities

- **Venetoclax**
  - R/R CLL including 17p del

- **Cotellic + Zelboraf**
  - BRAFmut melanoma

- **Alecensa**
  - 2L ALK+ lung cancer

- **Atezolizumab**
  - 2L+ lung and bladder cancer

- **Emicizumab (ACE910)**
  - Hemophilia A

- **Lebrikizumab**
  - Severe Asthma

- **Ocrelizumab**
  - RMS/ PPMS

- **Lampalizumab**
  - Geographic atrophy

- **Gazyva**
  - Refractory iNHL (GADOLIN)

- **Perjeta + Herceptin**
  - eBC HER2+ (APHINITY)

- **Gazyva**
  - 1L aNHL (GOYA)

- **Actemra**
  - Giant cell arteritis

- **Atezolizumab + Avastin**
  - 1L RCC

- **Gazyva**
  - 1L iNHL (GALLIUM)

- **Gazyva**
  - 1L ALK+ NSCLC

---

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

**Biosimilars**
MabThera, Herceptin, Avastin
## 2016 outlook

<table>
<thead>
<tr>
<th>Category</th>
<th>Outlook</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</td>
</tr>
<tr>
<td>Dividend outlook</td>
<td>Further increase dividend in Swiss francs</td>
</tr>
</tbody>
</table>

\(^1\) At Constant Exchange Rates (CER)
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></td>
<td>Low to medium</td>
</tr>
<tr>
<td></td>
<td>Cotellic/Zelboraf</td>
<td>Melanoma</td>
<td></td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Venetoclax</td>
<td>Hematology (CLL 17p del)*</td>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>2016</td>
<td>Ocrelizumab</td>
<td>Multiple Sclerosis</td>
<td></td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>Atezolizumab</td>
<td>NSCLC, bladder (2/3L)</td>
<td></td>
<td>Medium</td>
</tr>
<tr>
<td></td>
<td>Lebrikizumab</td>
<td>Asthma, AD, IPF, COPD</td>
<td></td>
<td>Large</td>
</tr>
<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>
</tr>
<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>

**Legend:**
- **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

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
Doing now what patients need next
Hemophilia A: There are significant limitations of current treatment options

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

**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*