Roche in Japan – A Challenging and Rewarding Experience of a Major Swiss Pharmaceutical Company

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Chief Medical Officer
F. Hoffmann – La Roche AG

23 October 2007
Roche and Japan – Brief historical review: 1899 to 2001

Roche – Global player in pharmaceutical industry

Growing challenges in pharmaceutical industry

The Chugai-Roche response: Meeting high medical needs in Japan

Outlook
Roche in Japan - 1

A rich history of successful collaboration

1899: Roche establishes network of sales representatives in Japan as first western pharmaceutical company

1904 Karl Rhode Company distributes Roche products in Japan

1912 Dr. E.C. Barell visits Japan; first Medical Representative system in Japan

1924 Roche opens its own company in Japan on July 7 under name of Roche Gomeikaisha

1932 Nippon Roche K.K. founded
“I arrived in Kobe on August first in 1926 after a journey of 35 days”

“I liked it in Japan from the beginning. The people were friendly, the country I found beautiful…”
Roche in Japan - 2

A rich history of successful collaboration

1950  First import licences for Roche products regained, e.g. for Saridon
1967  Kamakura factory completed
1972  Research center opened in Kamakura
1986  Rocaltrol in osteoporosis
1987  Furtulon anticancer drug
1992  Roferon-A alpha interferon as first treatment for HCV in Japan
1993  - Cefyl tablets introduced, an oral antibiotic
       - Bactramin injection introduced, a carini pneumonia drug
Roche in Japan - 3

A rich history of successful collaboration

1995  Vesnoid for acute promyelocytic leukemia

1996-2000  Four new drugs for HIV/AIDS, e.g. HIVID, Saquinivir

1999  CellCept for rejection reactions in patients with organ transplants

2001  - Promotion of Kytril for anti-nausea
       - Tamiflu for A-Type/B-Type influenza
       - Herceptin, a monoclonal antibody in metastatic breast cancer
       - Mabthera/Rituxan, a monoclonal antibody, in B-cell non-Hodgkin's lymphoma

2002  Roche acquires 50.1% of Chugai and merges its Japanese business with Chugai
Global Reach of Pharma Development

Benefiting from top-class expertise from around world

Roche PD Staff Total: ~3,500, excluding contractors, Genentech and Chugai

United Kingdom (Welwyn)

USA (NJ)

USA (CA)

Genentech (USA)

Switzerland (Basel)

Chugai (Japan)

China (Shanghai)
Delivering Clinically Differentiated Medicines
Succeeding across all 3 strategic objectives

First-in-Class
- Avastin in cancer
- Fuzeon in HIV
- Invirase in HIV
- Herceptin in BC
- Mabthera in NHL
- Actemra in RA
- Mabthera in RA
- Ocrelizumab in RA

Best-in-Class
- Pegasys in HCV and HBV
- Xeloda in cancer
- Boniva in osteoporosis
- Tarceva in cancer
- CERA in anemia

Lifecycle Development
- Mabthera
- Xeloda
- Avastin
- Tarceva
- Herceptin
- Pegasys
- Boniva

- Completed
- In Phase III
- Additional indications in Phase III
Roche Group’s Successful Track Record

Major progress in key disease areas

• We have achieved the Winning for the Future financial target of **doubling** Total Shareholder Return (TSR) value of Roche from 2002–2007

• We are market leaders in disease areas where we want to play:

**From 2002**
- Number 2 in oncology
- Number 2 in renal anemia*
- Number 2 in transplantation
- Number 5 in hepatitis
- Number 1 in obesity
- Number 4 in influenza
- Number 5 in HIV/Aids

**To 2007**
- Number 1 in oncology
- Number 1 in renal anemia*
- Number 1 in transplantation
- Number 1 in hepatitis
- Number 1 in obesity
- Number 1 in influenza
- Number 5 in HIV/Aids

Source: Extended Wood Mackenzie's Pharmaview, Jan 2007

* NeoRecormon territories
Pharmaceutical Industry Ranking in 2006

Roche moves up to #5 from #8

1. Pfizer
2. GlaxoSmithKline
3. Sanofi-Aventis
4. Novartis
5. Roche
6. AstraZeneca
7. Johnson & Johnson
8. Merck & Co.
9. Wyeth
10. Eli Lilly

Source: Extended Wood Mackenzie’s Pharmaview, August 2007
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Outlook
• Global pharmaceutical market will more than double to $1.3 trillion by 2020
• Drugmakers’ R&D spending in the US reached $55.2 billion in 2006
• FDA approved about half as many new treatments that year as a decade earlier
• Up to 45 percent of late-stage drugs currently fail
• Industry’s core problem is lack of innovation in making effective new therapies for the world’s unmet medical needs while R&D costs as well as marketing costs are increasing

➢ „Industry’s current business model is both economically unsustainable and operationally incapable of acting quickly enough to produce the types of innovative treatments that will be...“

by Daniel Beaulieu
Innovation Challenge
A gap in R&D productivity

Source: CMR International & IMS Health
Cost Challenge of Developing New Drugs

Significant increase in investment needed

R&D Productivity Challenge

Decreasing in USA

Source: BioExecutive International April 2007
Japan - Market Challenge

Positive and negative factors impacting the market

<table>
<thead>
<tr>
<th>Factors Negatively Impacting Market</th>
<th>Factors Positively Impacting Market</th>
</tr>
</thead>
<tbody>
<tr>
<td>• April 2007 NHI Price revisions</td>
<td>• Aging population driving growth in geriatric related therapies</td>
</tr>
<tr>
<td>• -6.7% on annual basis</td>
<td>• including Alzheimer’s, Parkinson’s and dementia</td>
</tr>
<tr>
<td>• -4.9% impact Q2-Q4 2007</td>
<td>• Continued growth in oncology</td>
</tr>
<tr>
<td>• Slowed volume growth</td>
<td>• +11.7% volume growth</td>
</tr>
<tr>
<td>• +3.2% in 2006 vs +6.2% in 2005</td>
<td>• est. 28% of all deaths</td>
</tr>
<tr>
<td>• Influenza season back to normal</td>
<td>• Expanding diabetes market</td>
</tr>
<tr>
<td>• -7.4% change in related Rx</td>
<td>• +8.9% volume increase</td>
</tr>
<tr>
<td>• Less severe pollinosis / allergy season</td>
<td>• MHLW est. 5.8% of population having and 6.9% at high risk</td>
</tr>
<tr>
<td>• -10.1% change in related Rx</td>
<td>• Growth in cardiovascular franchise</td>
</tr>
<tr>
<td>• Increased use of generics</td>
<td>• +8.4% volume increase</td>
</tr>
<tr>
<td>• including Cephalosporins, Statins, Antifungals, and Oral Antidiabetics</td>
<td></td>
</tr>
</tbody>
</table>
Japan: Availability of Recently Launched NCEs

25% of top 100 global products and 75% of NCEs not available in Japan

Of 142 NCEs launched globally between 2002 and 2006, 73 are available in Japan, only 32 launched in Japan.

Of top 100 products by global sales in 2006, 73 are available in Japan.

Source: IMS Health, IMS World Review 2005 and IMS MIDAS Quantum
Japan: Launch Lag between First Country of Launch and Japan Launch

**Approval times hover around 17-18 months**

<table>
<thead>
<tr>
<th>Product</th>
<th>Corp</th>
<th>1st Launch</th>
<th>Japan Launch</th>
<th>Months Lag</th>
<th>Average Approval Time in Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blopress</td>
<td>TAK</td>
<td>10/1997</td>
<td>6/1999</td>
<td>20</td>
<td>33.5 months for the 58 products approved in 1999</td>
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<tr>
<td>Aricept</td>
<td>EIS</td>
<td>1/1997</td>
<td>11/1999</td>
<td>34</td>
<td>28.3 months for the 67 products approved in 2000</td>
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<tr>
<td>Lipitor</td>
<td>PFZ</td>
<td>1/1997</td>
<td>5/2000</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Tamiflu</td>
<td>CHG</td>
<td>10/1999</td>
<td>2/2001</td>
<td>16</td>
<td>16.8 months for the 39 products approved in 2001</td>
</tr>
<tr>
<td>Glivec</td>
<td>NVR</td>
<td>5/2001</td>
<td>12/2001</td>
<td>7</td>
<td></td>
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<tr>
<td>Zyprexa</td>
<td>LLY</td>
<td>10/1996</td>
<td>6/2001</td>
<td>56</td>
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<tr>
<td>Fosamax</td>
<td>B.I</td>
<td>11/1993</td>
<td>8/2001</td>
<td>93</td>
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<tr>
<td>Iressa</td>
<td>AZN</td>
<td>7/2002</td>
<td>7/2002</td>
<td>0</td>
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<tr>
<td>Claritin</td>
<td>SHC</td>
<td>2/1988</td>
<td>9/2002</td>
<td>175</td>
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<tr>
<td>Pegasys</td>
<td>CHU</td>
<td>9/2001</td>
<td>12/2003</td>
<td>27</td>
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<tr>
<td>Evista</td>
<td>CHG</td>
<td>1/1998</td>
<td>5/2004</td>
<td>76</td>
<td>17.9 months for the 31 products approved in 2004</td>
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<tr>
<td>Bi Sifrol</td>
<td>B.I</td>
<td>7/1997</td>
<td>1/2004</td>
<td>78</td>
<td></td>
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<tr>
<td>Crestor</td>
<td>AZN</td>
<td>2/2003</td>
<td>4/2005</td>
<td>26</td>
<td></td>
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<tr>
<td>Zoloft</td>
<td>PFZ</td>
<td>12/1990</td>
<td>7/2006</td>
<td>187</td>
<td></td>
</tr>
</tbody>
</table>

Source: IMS Health, IMS MIDAS Quantum
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Outlook
Chugai-Roche Strategic Alliance
High-visibility partnership benefits both companies

December, 2001: Signing of Basic Agreement
October, 2002: Completion of merger with Nippon Roche and full--fledged start of the Alliance
Chugai-Roche “Unique” Alliance
Win-win opportunity for both partners

- Roche acquired 50.1% of Chugai shares
- Chugai and Nippon Roche merged
- Chugai maintained autonomous management

Win for Chugai
- Secures foundation for drug discovery technology related to bio-pharmaceuticals
- Acquires more chances to produce innovative products through R&D synergies
- Strengthens total resources, including product/pipeline portfolios
- Gains an option to the global market through Roche’s infrastructure

Win for Roche
- Acquires local management that understands the Japanese business environment
- Strengthens its presence in Japan - the world’s second largest market
- Increases opportunities to acquire Japan-originated innovative drugs
- Establishes a “Global Management Network” infrastructure (Hub & Spokes)
Japan: Ongoing M&A Shakes Up Top 10 in Japan

**Daiichi - Sankyo set to be new #1**

**2000 Rank**
- Sankyo
- Takeda
- Daiichi
- Yamanouchi
- Eisai
- Pfizer
- Shionogi
- Banyu
- Otsuka
- Novartis
- Chugai
- Tanabe
- Ono
- Fujisawa
- Sumitomo
- Glaxo Wellcome
- Aventis
- Welfide
- Kyowa Hakko
- Bayer

**2006 Rank**
- Pfizer
- Takeda
- Chugai
- Astellas
- Novartis
- Eisai
- Daiichi
- Sankyo
- GSK
- Dainippon Sumitomo
- Otsuka
- Mitsubishi
- AZ
- Banyu
- Shionogi
- Tanabe
- Ono
- Nippon Boehringer
- Sanofi-Aventis
- Taiho

**Estimated Rank**
- Daiichi-Sankyo
- Pfizer
- Takeda
- Mitsubishi-Tanabe
- Chugai
- Astellas
- Novartis
- Eisai
- GSK
- Dainippon Sumitomo
- Otsuka
- AstraZeneca
- Banyu
- Shionogi
- Ono
- Bayer-Schering
- Nippon Boehringer
- sanofi-aventis
- Taiho
- Kyowa Hakko

< Co's Outside Top 20 >

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Source: IMS Japan K.K., Japan Pharmaceutical Market (JPM)
Growth Performance across Franchises in Japan

**Oncology continues strong growth in 2006**

Franchise 2006 Growth (%) and 2001-2005 CAGR (%)

- Oncology
- Cardiovascular
- CNS
- Diabetes
- Gastro / Metabolism
- Arthritis & Pain
- Respiratory
- Anti-Infectives & Anti-Virals

Source: IMS Japan K.K., Japan Pharmaceutical Market
Areas of Focus and Products in Japan Market

Strong Chugai and Roche partnership

- Others: Rohypnol, Amoban, Ulcerlimin, Euglucon
- Infection/Transp Immunology: Actemra, Tamiflu, Pegasys, Copegus*, Rocephin
- Cardio/Cerebro Vascular: Sigmart, Rythmodan, Preran
- Bone/Joint: Alfarol, Rocaltrol, Suvenyl, Evista

¥326 billion in 2006 (consolidated net sales)

Cancer: Furtulon, Xeloda, Neutrogin, Kytril, Rituxan, Herceptin, Avastin*

Immunology & Infection: others 9.3%, Immunology: others 9.3%

Bone: 12.8%

Renal: 23.4%

CV: 9.9%

Renal: Epogin, Oxarol, Renagel

- Copegus and Avastin were launched in 2007
### Roche R&D Pipeline Today

**A promising flow of new medicines, also available to Japan**

**Roche managed**

<table>
<thead>
<tr>
<th>NME</th>
<th>Note</th>
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<tbody>
<tr>
<td>R547</td>
<td>solid tumors</td>
</tr>
<tr>
<td>1507</td>
<td>solid tumors</td>
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<tr>
<td>1530</td>
<td>solid tumors</td>
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<tr>
<td>1645</td>
<td>solid tumors</td>
</tr>
<tr>
<td>7204</td>
<td>malignant melanoma</td>
</tr>
<tr>
<td>GEN</td>
<td>PARP inh - malignant melanoma</td>
</tr>
<tr>
<td>GEN</td>
<td>DM1 - mBC</td>
</tr>
<tr>
<td>GEN</td>
<td>hedgehog ant - cancer</td>
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<tr>
<td>GEN</td>
<td>anti-CD20 3rd gen – hem malig</td>
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<tr>
<td>GEN</td>
<td>IAP antag – cancer therapy</td>
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<tr>
<td>GEN</td>
<td>MEK inh – cancer therapy</td>
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<tr>
<td>GEN</td>
<td>ABT-263 – sol tumors &amp; hem malig</td>
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<td>GEN</td>
<td>ABT-899 – sol tumors</td>
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<td>GEN</td>
<td>CD40 Ab - NHL/MM/rel large B-CL</td>
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<td>CHU</td>
<td>CRC</td>
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<td>R7277</td>
<td>RA</td>
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<td>R3477</td>
<td>autoimmune diseases</td>
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<tr>
<td>R1646</td>
<td>pain</td>
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<tr>
<td>R7205</td>
<td>HCV</td>
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<td>R7128</td>
<td>HCV</td>
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<tr>
<td>R7227</td>
<td>HCV</td>
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<tr>
<td>R1511</td>
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<td>R7118</td>
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<tr>
<td>R1295</td>
<td>MS</td>
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<tr>
<td>R1450</td>
<td>Alzheimer’s depression</td>
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<tr>
<td>R1647</td>
<td>Alzheimer’s schizophrenia</td>
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<tr>
<td>R1678</td>
<td>schizophrenia</td>
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<td>R4996</td>
<td>Alzheimer’s schizophrenia</td>
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<td>R547</td>
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<td>R7277</td>
<td>RA</td>
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<td>autoimmune diseases</td>
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<td>R4996</td>
<td>Alzheimer’s schizophrenia</td>
</tr>
</tbody>
</table>

**Status as of September 7, 2007**
Agenda

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Roche – Global player in pharmaceutical industry

Roche and Chugai – Bold strategic move toward a leadership position in Japan

The Roche/Chugai response to high medical needs in Japan – A strong portfolio

Outlook
Major Roche-Managed Projected Submissions
Portfolio variety expands over coming years

Status as of September 30, 2007
Unless stated otherwise, submissions will occur in US and EU
Future Regulatory Submissions in Japan
Filings reflect increasing global harmonization

- File for approval of NMEs and additional indications every year
- Secure safety and proper market introduction of new drugs

* overseas product name

<table>
<thead>
<tr>
<th>Year</th>
<th>New Molecular Entity</th>
<th>Additional Indication etc.</th>
<th>In-licensed from Roche</th>
</tr>
</thead>
<tbody>
<tr>
<td>~2006</td>
<td></td>
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<tr>
<td>2007</td>
<td>EPOGIN CIA</td>
<td>XELODA Adj.CC</td>
<td>AVASTIN CRC</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>COPEGUS HCV</td>
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<tr>
<td>2008</td>
<td>HERCEPTIN Adj.BC</td>
<td>TARCEVA* NSCLC</td>
<td>AVASTIN NSCLC</td>
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<td></td>
<td></td>
<td>ACTEMRA RA/Overseas</td>
<td>HERCEPTIN GC</td>
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<td>2009</td>
<td></td>
<td>XELODA CRC</td>
<td>AVASTIN BC</td>
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<td></td>
<td>HERCEPTIN GC</td>
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<td>2010~2012</td>
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<td>MIRCERA* CIA</td>
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<td>MIRCERA* Renal Anemia</td>
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<tr>
<td></td>
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<td></td>
<td>PEG/COPE Osteoporosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>BONVIVA* Osteoporosis</td>
</tr>
</tbody>
</table>

Launched in 2007
Thank you