Roche Pharma Development
Guido Magni
Global Head of Medical Sciences

Roadshow London, September 6th, 2006
This presentation contains certain forward-looking statements. These forward-looking statements may be identified by words such as 'believes', 'expects', 'anticipates', 'projects', 'intends', 'should', 'seeks', 'estimates', 'future' or similar expressions or by discussion of, among other things, strategy, goals, plans or intentions. Various factors may cause actual results to differ materially in the future from those reflected in forward-looking statements contained in this presentation, among others:

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.

Any statements regarding earnings per share growth is not a profit forecast and should not be interpreted to mean that Roche's earnings or earnings per share for this year or any subsequent period will necessarily match or exceed the historical published earnings or earnings per share of Roche.

For marketed products discussed in this presentation, please see full prescribing information on our website – www.roche.com

All mentioned trademarks are legally protected

Overview on value adding propositions

Roche in oncology
Roche in rheumatoid arthritis
Poised to re-enter cardiovascular and metabolic diseases

Summary
Appendix
H1 '06: Sales outgrowing market over three times

Highest increase in operating profit\(^1\) ever

- Oncology franchise continues to grow rapidly (+48 %\(^2\))
- Autoimmune franchise starting off in Europe and US following approval of MabThera/ Rituxan in first RA indication
- Boniva continues successful rollout in US, already 42 countries launched
- Operating profit\(^1\) increased 35 %\(^2\)
- 11 approvals received, 11 filings submitted
- Six phase III trials met primary endpoint
- Four phase II trials met primary endpoint

\(^1\) before exceptional items  \(^2\) local growth

H1 '06: Progress report on a leading late stage pipeline

<table>
<thead>
<tr>
<th>Phase III results</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mircera - renal anemia in dialysis patients (AMICUS)</td>
<td>Filed EU and US April '06</td>
</tr>
<tr>
<td>Mircera - renal anemia in pre-dialysis patients (ARCTOS)</td>
<td>Filed EU and US April '06</td>
</tr>
<tr>
<td>Xeloda – gastric Ca (ML17032)</td>
<td>Filing H2’ 06</td>
</tr>
<tr>
<td>Xeloda – oesophagogastric Ca (REAL2)</td>
<td>Filing H2’ 06</td>
</tr>
<tr>
<td>Actemra – RA (Japanese S&amp;S)</td>
<td>Filed Jp April ’06</td>
</tr>
<tr>
<td>Herceptin – mBC combo hormonal (TAnDEm)</td>
<td>Filing EU H2’ 06</td>
</tr>
<tr>
<td>Herceptin – adjuvant BC (HERA FU)</td>
<td>Approved EU H1’06</td>
</tr>
<tr>
<td>MabThera – RA TNF IR (REFLEX FU)</td>
<td>Approved EU and US H1 ’06</td>
</tr>
<tr>
<td>Avastin – pancreatic Ca (CALGB 80303)</td>
<td>AVITA continues, Filing EU ’08</td>
</tr>
<tr>
<td>Bondronat – Metastatic Bone Pain</td>
<td>Stopped due to slow recruitment</td>
</tr>
</tbody>
</table>

\(^1\) before exceptional items  \(^2\) local growth
**H1 '06: Progress report on early stage pipeline**

*Major additions to support growth beyond 2010/2015*

<table>
<thead>
<tr>
<th>Phase II results</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocrelizumab - RA (Action)</td>
<td>Phase III to start soon</td>
</tr>
<tr>
<td>Avastin + Tarceva - NSCLC 2nd line</td>
<td>Phase III ongoing</td>
</tr>
<tr>
<td>R1058 – dyslipidemia (efficacy)</td>
<td>Safety phase II trial ongoing</td>
</tr>
<tr>
<td>Ipsen BIM 51077 – T2D</td>
<td>Opted in, phase II (sustained release formulation) to start early '07</td>
</tr>
<tr>
<td>Insulin sensitizer – T2D</td>
<td>Discontinued</td>
</tr>
</tbody>
</table>

**Phase I progress**

5 new entries (moved from phase 0 or newly entered)
- R194 – dyslipidemia
- R140 – Alzheimer’s
- R107 – solid tumors
- Trastuzumab DM1 (GNE) – mBC
- R2A77 (SIP1, Actelion) – autoimmune diseases

2 moved forward to phase II
- Topical VEGF (GNE) – diabetic foot ulcers
- Opt-in (ARQ 501) – solid tumors

3 terminated
- Raptiva (GNE) – adult atopic dermatitis
- CHC 12103 (CHU) – solid tumors
- R1508 (Antiutero) – mBC

*partnered in July '06

---

**An industry leading late stage pipeline**

*Again strengthened*

**Phase III/ filed projects**

<table>
<thead>
<tr>
<th>FY '05</th>
<th>approved</th>
<th>discontinued</th>
<th>new entries</th>
<th>HY '06</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>8*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>41</td>
<td></td>
</tr>
</tbody>
</table>

*Including one project previously combined and now listed as two single indications
As of June 30, 2006
### Roche: Existing and future pillars of growth

#### Oncology
- **MabThera**
- **Avastin**
- **Herceptin**
- **Tarceva**
- **Omnitarg**
- **Mircera**
- **Oncology**
- **Xeloda**
- **CellCept**
- **Actemra**
- **R1492**
- **ARQ**
- **4 phase I compounds**

#### RA/ Autoimmune
- **MabThera**
- **Actemra**
- **CellCept**
- **R1503** p38 kinase inh.
- **R1584** Ran anti CD-20
- **4 phase I compounds**

#### Metabolic
- **R1440**
- **R1638**
- **R1658 (JTT-705)**
- **GLP-1**
- **3 phase I compounds**

#### Neurology/ Psychiatry
- **4 phase I compounds**
- **4 phase II compounds**

---

### Overview on value adding propositions

#### Roche in oncology

#### Roche in rheumatoid arthritis

Poised to re-enter cardiovascular and metabolic diseases

#### Summary

#### Appendix
Leadership in oncology achieved in five years
Success through life-extending medicines

Maximizing the potential of our assets
Taking proven drugs into new markets

Low risk expansion
across tumour types

Innovative
development

medically
DIFFERENTIATED
products

in adjuvant & metastatic settings
Herceptin in BC, Tarceva in NSCLC

in combination with current
and future ‘regimes’
Breast: Taxol, Taxotere, Xeloda
Lung: Taxol, Gemcitabine, combo targeted therapies

Avastin in CRC, BC, NSCLC, RCC, Pancreatic Ca,
Ovarian Ca, Prostate Ca

CHF bn
2000 2001 2002 2003 2004 2005
MabThera
Herceptin
Xeloda
Avastin
Kytril
Bondronat
NeoRecorm.

Roche Pharmaceuticals Division

Roche
A rich phase III pipeline targeting all main tumor types and early intervention

<table>
<thead>
<tr>
<th>ADJUVANT MAINT.</th>
<th>1st LINE</th>
<th>2nd LINE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Filed or to file soon</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xeloda adjuvant BC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avastin mCRC 1st line ext.</td>
<td>Avastin mCRC 1st line ext.</td>
<td>Avastin mCRC combo hormone</td>
</tr>
<tr>
<td>Avastin mCRC 1st line ext.</td>
<td>Herceptin gastric Ca</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Ongoing</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Xeloda adjuvant BC</td>
<td>Tarceva &amp; Avastin NSCLC maintenance</td>
<td></td>
</tr>
<tr>
<td>Avastin adjuvant rectal Ca</td>
<td>Avastin pancreatic Ca</td>
<td></td>
</tr>
<tr>
<td>Avastin pancreatic Ca</td>
<td>Avastin mCRC 1st line ext.</td>
<td>Herceptin gastric Ca</td>
</tr>
<tr>
<td>Avastin pancreatic Ca</td>
<td>MabThera relapsed CLL</td>
<td>Xeloda mCRC 2nd line combo</td>
</tr>
<tr>
<td>Avastin ovarian Ca</td>
<td>Tarceva &amp; Avastin NSCLC 2nd line</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>To start soon</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tarceva adjuvant NSCLC</td>
<td>ialogue on value adding propositions</td>
<td></td>
</tr>
<tr>
<td>Avastin adjuvant NSCLC</td>
<td>Roche in oncology</td>
<td></td>
</tr>
<tr>
<td>Avastin adjuvant BC</td>
<td>Roche in rheumatoid arthritis</td>
<td></td>
</tr>
</tbody>
</table>

Full update on activities in oncology given at Roche Oncology Day, June 19, 2006

Overview on value adding propositions

Roche in oncology

Roche in rheumatoid arthritis

Poised to re-enter cardiovascular and metabolic diseases

Summary

Appendix
Roche in RA
*Poised for a leadership role*

**MabThera / Rituxan (rituximab)**
- Launched in RA anti-TNF inadequate responders in US and EU
- Phase III in RA DMARD inadequate responders ongoing
- Phase III for repeated treatment courses ongoing

**Actemra (tocilizumab)**
- Japanese phase III in DMARD inadequate responders met primary endpoints - filed in Japan
- Phase III in RoW ongoing

**Ocrelizumab**
- First phase II trial met primary and secondary endpoints
- Phase III program to be finalized and initiated soon

**R1503**
- Phase II initiated in Q4’05

---

**REFLEX: Randomised Evaluation of Long-term Efficacy of MabThera in RA**

- Multi-centre, randomized, double-blind, placebo-controlled phase III study enrolling 514 patients
- Primary Endpoint:
  - proportion of patients with an ACR20 response at Week 24
- Secondary and exploratory radiographic endpoints:
  - secondary: Change in modified Sharp radiographic total score, erosion score, and joint space narrowing score at Week 56
  - exploratory: Change in modified Sharp radiographic total score, erosion score, and joint space narrowing score at Week 24
Significant ACR responses at Week 24

**REFLEX**

![Bar chart showing ACR responses at Week 24](chart1.png)


---

Significant inhibition of radiographic progression at Week 56

**REFLEX**

![Bar chart showing radiographic progression](chart2.png)

Primary Analysis: Radiographs within time window, linear extrapolation from Week 24 for missing values

Keystone et al, EULAR 2006 (Abstract No. OPO016)
Summary and outlook

**MabThera/ Rituxan**

- Data from the REFLEX study provide first indication that a B cell-targeted therapy can inhibit radiographic progression
  - also represent first significant evidence of inhibition of radiographic progression in patients with an inadequate response to 1 or more TNF inhibitors
- Repeated courses of MabThera treatment show similar or improved efficacy compared with the first course with no change in the safety profile
- Further phase III development program in patients with RA who have had an inadequate response to disease modifying anti-rheumatic drugs (DMARDs) ongoing
  - enrolling more than 1,700 patients
  - recruitment started end 2005/early 2006
  - all trials including a repeated treatment course after six months
  - EU filing planned in 2008

**Actemra**

**Japanese phase III results**

- Humanized anti-human interleukin-6 (IL-6) receptor monoclonal antibody
- S&S trial (SATORI)
  - Phase III clinical trial, double-blind randomized, 125 patients who had an inadequate response to methotrexate, Actemra monotherapy vs. MTX
  - Primary Endpoint: improvement of ACR20 response at Week 24
- PJD trial (SAMURAI)
  - Phase III clinical trial, randomized trial, 306 patients with early active RA of less than 5 years, Actemra monotherapy vs. active comparator
  - Primary Endpoint: Sharp score at week 52
Strong ACR scores (SATORI)
Actemra shows consistent high efficacy

Actemra substantially reduces joints damage (SAMURAI)
Radiographic data, mean scores
Summary and outlook

**Actemra**

- Actemra monotherapy is **effective in controlling both**:  
  - signs and symptoms of RA (excellent ACR scores achieved)  
  - progression of structural damage
- The effectiveness of Actemra is **sustained over time**
- Actemra is in **general well tolerated**
- Already filed in Japan
- The **large phase III program being conducted in the US and Europe** is expected to confirm outstanding Japanese results - more than 4,000 patients to be enrolled  
  - filing planned for 2007
- Actemra, through its **novel mechanism of action**, might become soon a new option for patients suffering from RA

Overview on value adding propositions

**Roche in oncology**

**Roche in rheumatoid arthritis**

**Poised to re-enter cardiovascular and metabolic diseases**

**Summary**

**Appendix**
**Global burden of cardiovascular disease**

*Clinical care of CVD is costly and prolonged*

In 2002

- CVD contributed to approximately one-third of all global deaths (17 million)
- 80% of burden is in low- and middle-income countries

By 2020

- CHD and stroke will become the leading causes of death and disability worldwide
- Mortality from CVD will increase to 20 million

---

**CETP inhibition as a novel strategy to raise HDL**

[Diagram showing CETP inhibition process]

---

**Abbreviations**

- ABCA1: ATP-binding cassette, sub-family A
- A-I: apolipoprotein 1
- CE: cholesteryl ester
- CETP: CE transfer protein
- FC: free cholesterol
- HDL: high-density lipoprotein
- LDL: low-density lipoprotein
- LDLR: LDL receptor
- SR-BI: scavenger receptor class-B type I
- TG: triglyceride

---

*International Cardiovascular Disease Statistics 2003, 2005, AHA*

1 Men aged 35-74 years  
CHD: coronary heart disease
Phase IIa PoC studies

- **Phase II study in healthy subjects with mild hyperlipidemia (N=198)**
  - 0, 300, 600, 900 mg qd for 4 weeks

- **Phase II study in subjects with Type II dyslipidemia (N=155)**
  - 0, 300, 600 mg qd with **pravastatin** 40 mg qd for 4 weeks

---

**JTT-705/ R1658 phase IIa data**

*Monotherapy*

---

**CETP activity**

- % change

**HDL-C**

- % change

---

*de Grooth GJ et al. Circulation 2002;105:2159-65*
**JTT-705/ R1658 in combination with pravastatin**

**Lipid effects**

![Graph showing lipid effects](image)

Pravastatin administered for 12 weeks; JTT-705 administered for the last 4 weeks


---

**Phase IIb efficacy and safety profile**

- Two clinical trials initiated, one completed
- JTT-705/ R1658 up to 900 mg daily is well-tolerated, with a similar overall safety profile to placebo
- Most frequently reported adverse events were mild GI symptoms (e.g. diarrhea, nausea) which did not lead to discontinuation of treatment
- No increase in blood pressure observed (consistent with pre-clinical findings)
- Phase IIb **safety trial** continues, data expected in 2007

Summary and outlook

**JTT-705/ R1658**

- Roche and Japan Tobacco signed agreement for development and commercialization of CETP inhibition in hyperlipidemia/dyslipidemia in October 2004
  - Roche has exclusive worldwide rights, excluding Japan and Korea
- Clinical efficacy data confirms benefits of CETP inhibition in hyperlipidemia/dyslipidemia
- Well-tolerated, with a similar overall safety profile to placebo
- Phase II in dyslipidemia (combination with pravastatin)
  - primary endpoint: percentage and absolute change from baseline at Week 12 in HDL-C level (efficacy)
  - already seen encouraging efficacy data
  - safety trial ongoing
  - go/ no go decision for phase III in 2007

---

Global prevalence of diabetes

**Strongly driven by obesity and ageing**

**Estimated number of people with diabetes by region**

<table>
<thead>
<tr>
<th>Region</th>
<th>2000</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developed countries</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latin America</td>
<td></td>
<td></td>
</tr>
<tr>
<td>India &amp; China</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Asia, Africa</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Major healthcare challenge**

- Expanding prevalence > 350 mio by 2030
- Causing a number of vascular complications
- Significant burden to healthcare funding
- 50% of all diabetics are unaware of their condition
- Type 2 diabetes accounts for 85% - 95% of all diabetics

Source: Diabetes Care, Volume 27, May 2004
Type 2 Diabetes

Disease progression despite intensive therapy

- Multiple MOAs targeting underlying physiopathologies,
  - greater and long-term efficacy
- Compliance for oral anti-hyperglycemic agents (OHAs) estimated at 60-70% (US)
  - restricted due to side effects (weight gain, nausea, CHF)
- Combination therapy & fixed combos
- Disease-modifiers
- New developments

United Kingdom Prospective Diabetes Study

Cross sectional, median values

HbA1c (%)

0 3 6 9 12 15

0 3 6 9

Years from randomization

Conventional therapy

Intensive therapy

6.2% upper limit of normal range

Conventional: FPG <15 mmol/L diet, pharmacotherapy

Intensive: FPG <6 mmol/L (SUs, Metformin, insulin or combos)

Type 2 Diabetes

Therapeutic options

Current options

New options

- Sulfonfonyureas
- Repaglinide
- Nateglinide

PANCREAS

Impaired insulin secretion

Glucose

HGO*

MUSCLE

↓ Glucose uptake

ADIPOSE TISSUE

↓ Glucose uptake

LIVER

GKA

DPP-IV

GKA

DPP-IV

Hyperglycemia

↑ Glucose uptake

GUT

Metformin

Acarbose

Miglitol

*DGO = hepatic glucose output.
Glucagon-like peptide (GLP-1)

**Important therapeutic target for type 2 diabetes**

- Incretin hormone, produced by L-cells of intestine in response to food intake
- Dual mechanism of action: stimulates insulin secretion, inhibits glucagon release
- Induces pancreatic β-cell proliferation/differentiation
- Delay in gastric emptying and appetite suppression
- Short half life: rapidly broken down by dipeptidyl peptidase (DPP IV)
  - protection against hypoglycemia
- Reduced GLP-1 response to food in T2D patients

BIM-51077/ R1583: Partnered with Ipsen

**Data published**

**Immediate release formulation**

- Phase II: 28 days of continuous s.c. infusion
- Demonstrated linear dose/response curve, good HbA1c lowering, good tolerability, trend to increase insulin secretion and decrease body weight and appetite
- Presented at ADA '06

**Sustained release formulation**

- Preclinical data in beagle dog: s.c. injection with a small needle
- Achieved sustained release profile and long duration of release
- Presented at ADA '06
BIM-51077/ R1583
Phase II 28 days continuous infusion

24h profile of blood glucose concentrations
Day 28, mean glucose concentration [mmol/L]

Summary and outlook
BIM-51077/ R1583 (GLP-1)

- Greater binding potency than native protein
- Extended metabolic half life (22-fold more stable in plasma)
- Sustained improvement in blood glucose control over days by continuous infusion
- Good safety profile, no antibodies against BIM-51077
- Significant and rapid effect on 24h blood glucose following infusion
  - effect maintained over 28 days without desensitization
- Sustained effect on fasting blood glucose over 28 days
- Trend to increase insulin secretion, to decrease HbA1c, and decrease body weight and appetite
- Opted-in July 2006, start of phase II (sustained release formulation) early '07
- Frequency of administration planned to study: once a week and beyond
Type 2 Diabetes

Dipeptidyl peptidase (DPP IV) inhibitors

- Protects GLP-1 from rapid degradation
- **Main benefits**
  - can be taken orally
  - potential for monotherapy and combination (sulfonylurea, metformin or glitazones)
- **Main disadvantages**
  - no weight loss
  - side effects?
  - ‘rich’ competitive environment

Summary and outlook

*R1438 (DPP –IV)*

- Potentially best in class molecule
- 2 phase II ongoing
  - mono and combo with metformin
  - to complete end 2006/ early 2007
  - filing planned in 2009
- Back-up compounds in earlier stages of development
**Type 2 Diabetes**

**Glucokinase Activator (GKAs)**

- Glucokinase: key enzyme regulating whole body glucose homeostasis
- Genetic loss of GK activity in humans leads to early diabetes
- GKAs address 2 of the underlying pathologies in T2D
  - impaired insulin secretion
  - increased liver glucose production

**Summary and outlook**

**R1440 (GKA)**

- First in class molecule
- Phase II ongoing in type II diabetes
  - four studies currently running (mono or combo with metformin, safety combo with sulfonylurea, titration study)
  - initiated in Q4’05
  - first data in 2007
  - filing planned in 2009

- Main benefits of this class
  - oral
  - addresses two underlying pathogenic mechanisms of type II diabetes
Overview on value adding propositions

Roche in oncology

Roche in rheumatoid arthritis

Poised to re-enter cardiovascular and metabolic diseases

Summary

Appendix

Our objectives for 2006 - Pharmaceuticals

Announced for 2006

<table>
<thead>
<tr>
<th>Compound</th>
<th>Phase</th>
<th>Indication</th>
<th>Data</th>
<th>Status H1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mircera (CERA)</td>
<td>III</td>
<td>Renal anemia (correction)</td>
<td>Final</td>
<td></td>
</tr>
<tr>
<td>CellCept</td>
<td>III</td>
<td>Lupus nephritis (Induction phase)</td>
<td>Final</td>
<td></td>
</tr>
<tr>
<td>Herceptin</td>
<td>III</td>
<td>mBC combo hormonal (TAnDEM)</td>
<td>Final</td>
<td></td>
</tr>
<tr>
<td>Xeloda</td>
<td>III</td>
<td>mCRC 2nd line</td>
<td>Final</td>
<td></td>
</tr>
<tr>
<td>Avastin</td>
<td>III</td>
<td>NSCLC 1st line (AVAIL)</td>
<td>Interim</td>
<td>✔</td>
</tr>
<tr>
<td>Avastin / Xeloda</td>
<td>III</td>
<td>mCRC 1st line combo extension</td>
<td>Final</td>
<td></td>
</tr>
<tr>
<td>R1658</td>
<td>II</td>
<td>Dyslipidemia</td>
<td>Final</td>
<td>✔</td>
</tr>
<tr>
<td>R873</td>
<td>Iia</td>
<td>MED</td>
<td>Final</td>
<td></td>
</tr>
<tr>
<td>Avastin / Tarceva</td>
<td>II</td>
<td>NSCLC 2nd line</td>
<td>Final</td>
<td>✔</td>
</tr>
<tr>
<td>R1594</td>
<td>II</td>
<td>RA</td>
<td>Final</td>
<td>✔</td>
</tr>
</tbody>
</table>

Major clinical data

<table>
<thead>
<tr>
<th>Filings</th>
<th>Compound</th>
<th>Indication</th>
<th>Status H1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mircera (CERA)</td>
<td>Renal anemia</td>
<td>✔</td>
</tr>
<tr>
<td></td>
<td>Avastin</td>
<td>NSCLC 1st line</td>
<td>✔ (US)</td>
</tr>
<tr>
<td></td>
<td>Avastin</td>
<td>mBC 1st line</td>
<td>✔</td>
</tr>
<tr>
<td></td>
<td>Avastin / Xeloda</td>
<td>mCRC 1st line extension</td>
<td>✔</td>
</tr>
<tr>
<td></td>
<td>Herceptin</td>
<td>Adjuvant BC</td>
<td>✔</td>
</tr>
<tr>
<td></td>
<td>Herceptin</td>
<td>mBC combo hormonal</td>
<td>✔</td>
</tr>
<tr>
<td></td>
<td>Xeloda</td>
<td>mCRC 1st line combo</td>
<td>✔</td>
</tr>
</tbody>
</table>

Divisional sales growth

Double-digit growth in local currencies

barring unforeseen events
Summary
Building additional value propositions

• Oncology - on hands
• Autoimmune diseases/ rheumatoid arthritis - in the 'late stage' of development/ launch
• Metabolic disease - a potential opportunity shaping up
• CNS - still in an early stage
Overview on value adding propositions

Roche in oncology

Roche in rheumatoid arthritis

Poised to re-enter cardiovascular and metabolic diseases

Summary

Appendix

Roche’s phase III program for MabThera in DMARD inadequate responders and MTX naïve patients

All trials including a repeated treatment course after six months

<table>
<thead>
<tr>
<th>Trial</th>
<th>Treatment</th>
<th>Sample Size</th>
<th>Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX-IR SERENE</td>
<td>MTX + placebo vs. MTX + MabThera 1g vs. MTX + MabThera 2g</td>
<td>495</td>
<td>Reduction in signs and symptoms</td>
</tr>
<tr>
<td>MTX naïve (X-ray study)</td>
<td>MTX vs. MTX + MabThera 1g vs. MTX + MabThera 2g</td>
<td>852</td>
<td>Reduction in signs and symptoms</td>
</tr>
<tr>
<td>MIRROR</td>
<td>Rituximab 1g retx 1g vs. Rituximab 1g retx 2g vs. Rituximab 2g retx 2g</td>
<td>375</td>
<td>Effect of further courses and dose escalation</td>
</tr>
</tbody>
</table>

Endpoints:
- Reduction in signs and symptoms
- Inhibition of structural joint damage
- Improvement in physical function

EU Filing 2008
Roche's phase III program for Actemra

*Five trials ongoing*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Sample Size</th>
<th>Patient population</th>
<th>Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actemra 4 mg + MTX Actemra 8 mg + MTX</td>
<td>630</td>
<td>MTX partial responders</td>
<td>ACR 20 response at Wk 24</td>
</tr>
<tr>
<td>Actemra 4 mg + MTX Actemra 8 mg + MTX MTX OPTION</td>
<td>T'178</td>
<td>MTX partial responders</td>
<td>ACR 20 at Wk 24</td>
</tr>
<tr>
<td>Actemra 4 mg + MTX Actemra 8 mg + MTX MTX TOWARD</td>
<td>T'209</td>
<td>DMARD partial responders</td>
<td>ACR 20 response at Wk 24</td>
</tr>
<tr>
<td>Actemra 8 mg + DMARDs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actemra 8 mg + MTX Actemra 8 mg + MTX</td>
<td>570</td>
<td>Anti-TNF failures</td>
<td>ACR 20 response at Wk24</td>
</tr>
<tr>
<td>Actemra 8 mg + MTX Actemra 8 mg + MTX MTX RADIATE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actemra 8 mg MTX AMBITION</td>
<td>550</td>
<td>MTX naive</td>
<td>ACR 20 response at Wk 24</td>
</tr>
</tbody>
</table>

**Filing 2007**

---

**H1 '06: 11 approvals in major markets**

*Pharmaceuticals Division*

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication</th>
<th>Region</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avastin</td>
<td>2nd line mCRC</td>
<td>US</td>
</tr>
<tr>
<td>Boniva/ Bonviva iv</td>
<td>Osteoporosis</td>
<td>US, EU</td>
</tr>
<tr>
<td>Herceptin</td>
<td>Adjuvant BC</td>
<td>EU</td>
</tr>
<tr>
<td>Femara</td>
<td>BC</td>
<td>Japan</td>
</tr>
<tr>
<td>Lucentis</td>
<td>AMD</td>
<td>US</td>
</tr>
<tr>
<td>MabThera/ Rituxan</td>
<td>Rheumatoid arthritis</td>
<td>US, EU</td>
</tr>
<tr>
<td>MabThera</td>
<td>iNHL maintenance</td>
<td>EU</td>
</tr>
<tr>
<td>Rituxan</td>
<td>1st line aNHL</td>
<td>US</td>
</tr>
<tr>
<td>Tamiflu</td>
<td>Influenza prophylaxis (ped.)</td>
<td>EU</td>
</tr>
</tbody>
</table>
A rich and low risk Phase III pipeline
Keeping the high level of commitment

Fled or to file soon

MabThera
Ra, macrolactam
Herceptin
adj. BC
Mircera (CERA) renal anemia
Avastin
gastrointestinal,
hepatitis, skin
Herceptin
mCRC combo bevacizumab
Antevas
chemotherapy-induced neutropenia

Ongoing

MabThera
1st line CLL
MabThera
related CLL
MabThera
mCRC 1st line
Avastin
tumor necrosis factor antagonist
Avastin
adj. BC
Avastin
gastrointestinal,
hepatitis, skin
Actemra
RA, sJIA
Tarceva
NSCLC 1st line chemo
Actemra
RA DMARD inadeq. resp.

CeliCept
IgA nephropathy
ED-71
osteoporosis
Actemra
RA DMARD inadeq. resp.

Xolair
pediatric asthma
MabThera
RA TNF nonresp.

To start soon

Tarceva
adj. NSCLC
Avastin
adj. BC

Avastin
mBC combo

√

√

√

√

√

√

√

√

Major Roche managed projected submissions over the next years

Phase II
Phase III

R:1598
bacterial infections
R:1492
solid tumors
MabThera
mCRC combo bevacizumab,
mpn (IL)
Avastin
pancreatic CI (III)
Herceptin
gastrointestinal,
hepatitis, skin
Avastin
adj. CC combo
Herceptin
gastrointestinal,
hepatitis, skin
Tarceva
NSCLC 1st line
Avastin
mBC combo

R:1503
RA
R:173
male erectile dysfunction
R:1994
RA (III)
R:857
empyema
R:1273
(omeprazole) solid tumors (III)
R:1658
dyslipidemia
R:1649
IgA deficiency
R:1438
type II diabetes
R:873
male erectile dysfunction
R:1503
RA (III)
R:1598
IgA deficiency
R:1438
type II diabetes
R:1658
dyslipidemia
Avastin
NSCLC squamous (III)
Avastin
adj. CC (III)
Avastin
ovarian Ca (III)
MabThera
RA DMARD inadeq. resp. (EU)

2006 2007 2008 2009 post 2009

Status as of June 30, 2006
Unless stated otherwise, submissions will occur in US and EU
Roche R&D pipeline today
Total of 57 NME's + 55 Additional Indications

Status as of June 30, 2006

Roche managed R&D pipeline - overview
Projects by Therapeutic Area

Research
Inflammatory, Autoimmune and Bone Diseases
Neurological and Psychiatric Diseases
Cardiovascular and Metabolic Diseases
Oncology

Development
Inflammatory, Autoimmune and Bone Diseases
Neurological and Psychiatric Diseases
Cardiovascular and Metabolic Diseases
Oncology

Status as of June 30, 2006
Cardiovascular disorders

Atherosclerosis

- Damage to the arterial wall (large or medium-sized arteries) and subsequent creation of plaque consisting of cholesterol on the damaged area (hardening of arteries)
- Can lead to coronary heart disease (CHD) and sudden death

Hypertension

- Systolic blood pressure of 140 mm Hg or above or diastolic blood pressure of 90 mm Hg or above
- Increases risk of heart attack, stroke and renal failure

Dyslipidemia

- Total cholesterol above 200 mg/dl, LDL cholesterol above 130 mg/dl
- Increased cholesterol level resulting in coronary arteries becoming clogged

Thrombosis

- Formation of blood clots in the blood system in the absence of bleeding
- Can arise following the rupture of an atherosclerotic plaque in arteries

JTT-705/ R1658

Preclinical evaluation

- A thiol ester
- Forms a disulfide bond with CETP at cys 13
- Human, rabbit, hamster, cynomolgus monkey, marmosets: plasma IC50 in vitro: 1 – 11.7 µM

Effect of JTT-705 on serum CETP activity in marmosets

Okamoto H et al. Eur J Pharmacol 2003;466:147-54
Marmoset picture: www.bristolzoo.org