Roche

We Innovate Healthcare

Roche

Roche Pharma Development

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UBS Global Life Science Conference, New York, September 25-26th, 2006

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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;
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
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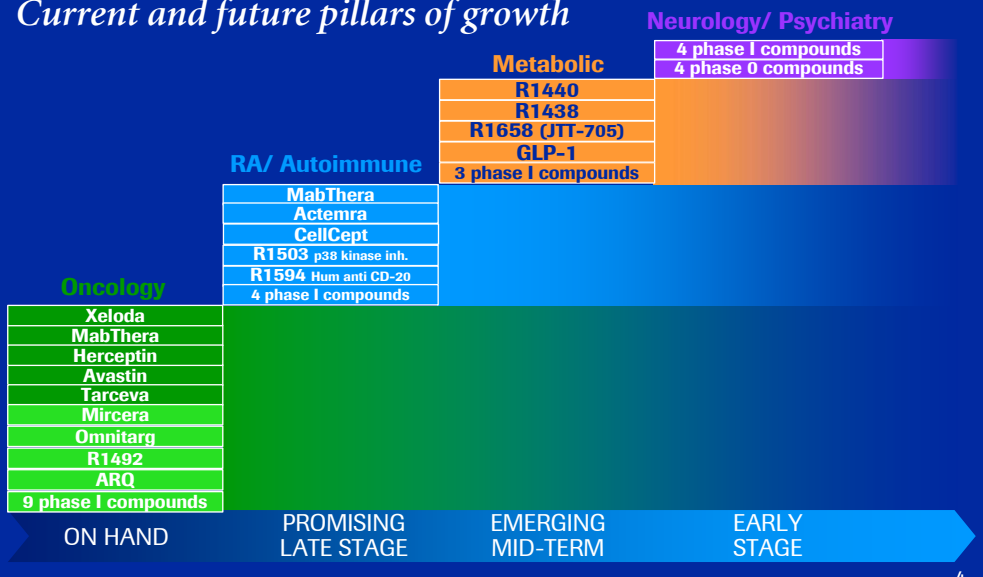
Roche key therapeutic areas

Current and future pillars of growth



Roche progress report H1'06

Leading late stage pipeline

	Phase III results	Status
✓	**Mircera** – renal anemia (AMICUS)	Filed EU and US April '06
✓	**Mircera** – renal anemia (ARCTOS)	Filed EU and US April '06
✓	**Xeloda** – gastric Ca (ML17032)	Filed July ' 06
✓	**Xeloda** – oesophagogastr. Ca (REAL2)	Filed July ' 06
✓	**Actemra** – RA (Japanese S&S)	Filed Jp April '06
✓	**Herceptin** – mBC combo hormonal (TAnDEM)	Filing EU H2' 06
✓	**Herceptin** – adjuvant BC (HERA FU)	Appr. EU H1'06
✓	**MabThera** – RA TNF IR (REFLEX FU)	Appr. EU and US H1 '06
-	**Avastin** – pancr. Ca (CALGB 80303)	AVITA continues, Filing EU '08
×	**Bondronat** - Metastatic Bone Pain	Stopped due to slow recruitment

	Phase II results	Status
✓	**Ocrelizumab** – RA (Action)	Phase III to start soon
✓	**Avastin + Tarceva** – NSCLC 2nd line	Phase III ongoing
✓	**R1658** – dyslipidemia (efficacy)	Safety phase II trial ongoing
✓	**Ipsen BIM 51077** – T2D	Opted in, phase II (sustained release formulation) to start early '07
×	***Insulin sensitizer*** – *T2D*	*Discontinued*

Oncology – the main current growth driver

Rheumatoid arthritis – emerging disease area for growth

Metabolic diseases – therapeutic area for future growth

Summary

Q&A

Maximizing the potential of our assets

Taking proven drugs into new markets

Innovative development

medically **DIFFERENTIATED** products

Low risk expansion

across tumour types

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

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

A rich phase III pipeline

Targeting main tumor types and use in early intervention

	ADJUVANT	MAINT.	1st LINE			2nd LINE	
Filed or to file soon			Tarceva pancreatic Ca ✓	Avastin NSCLC ✓	Avastin mBC ✓		
			Xeloda mCRC 1st line combo	Xeloda gastric Ca ✓			
			Avastin mCRC 1st line ext.	Herceptin mBC combo hormonal			
Ongoing	Xeloda adjuvant BC	Tarceva & Avastin NSCLC maintenance	Avastin RCC	Avastin mBC 1st line ext.	Herceptin gastric Ca	MabThera relapsed CLL	Xeloda mCRC 2nd line combo
	Xeloda adjuvant CC combo		Avastin pancreatic Ca	MabThera 1st line CLL		Avastin prostate Ca	Avastin mBC 2nd line
	Avastin adjuvant rectal Ca		Avastin ovarian Ca	Tarceva NSCLC 1st line		Tarceva & Avastin NSCLC 2nd line	
To start soon	Tarceva adjuvant NSCLC						
	Avastin adjuvant NSCLC						
	Avastin adjuvant BC						

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

Oncology – the main current growth driver

Rheumatoid arthritis – emerging disease area for growth

Metabolic diseases – therapeutic area for future growth

Summary

Q&A

Roche in rheumatoid arthritis
Positioned 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

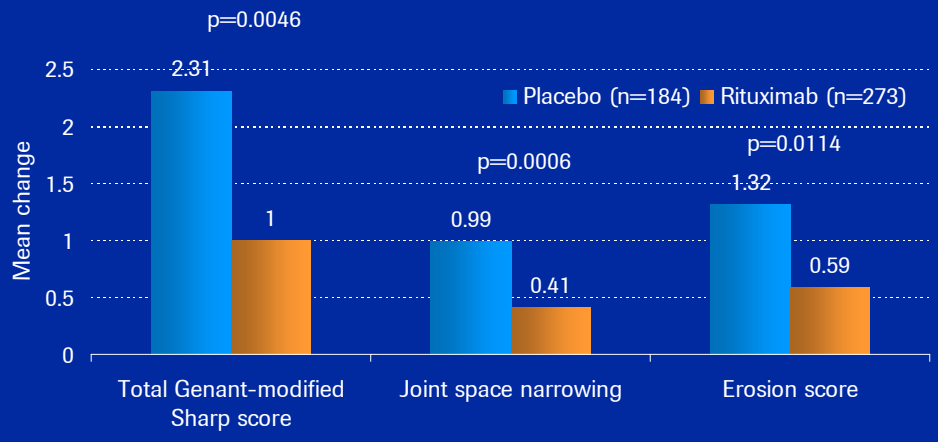
- First phase II trial met primary and secondary endpoints
- Phase III program to be finalized and initiated soon

R1503 (p38 kinase inhibitor)

- Phase II initiated in Q4'05

MabThera in RA: REFLEX (anti-TNF inadequate responders)

Significant inhibition of radiographic progression at Week 56



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

MabThera/ Rituxan

Summary and outlook

- REFLEX study provides first indication that a B cell-targeted therapy can inhibit radiographic progression
  - also demonstrates for the first time 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 treatment course with no change in the safety profile
- Phase III development program in patients with RA who have had an inadequate response to disease modifying anti-rheumatic drugs (DMARDs) ongoing
  - recruitment started end 2005/early 2006
  - Enrollment of more than 1,700 patients ongoing
  - EU filing planned in 2008

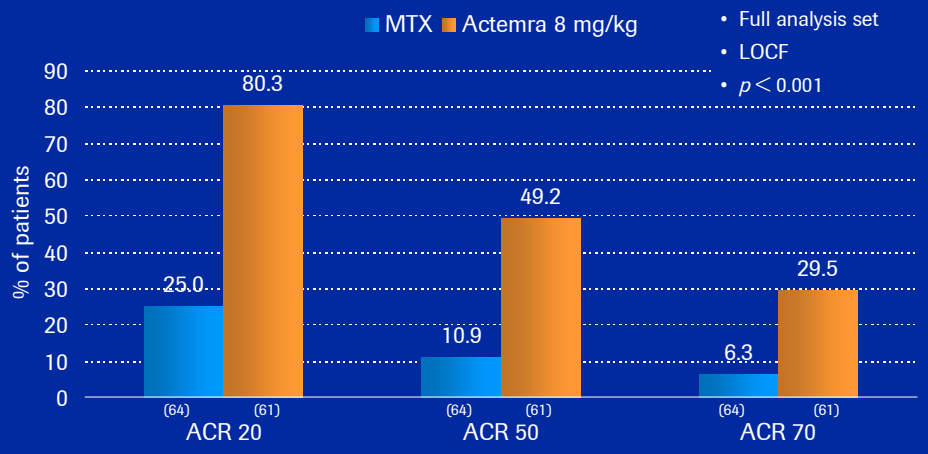
Actemra in RA

Japanese phase III results

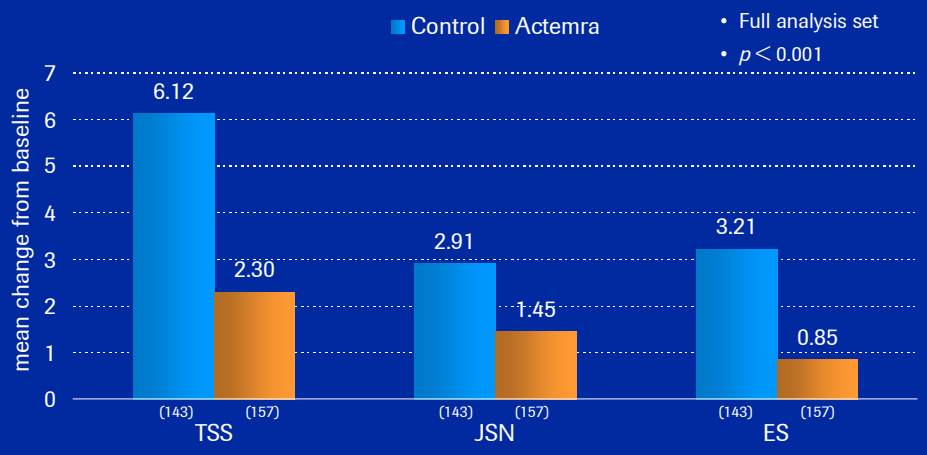
- Humanized anti-human interleukin-6 (IL-6) receptor monoclonal antibody
- S&S trial (SATORI)
  - Phase III clinical trial, double-blind randomized, 125 patients who had an inadequate response to methotrexate, Actemra monotherapy vs. MTX
  - Primary Endpoint: improvement of ACR20 response at Week 24
- 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

Actemra in RA: SATORI, S&S study

High ACR scores



Actemra in RA: SAMURAI, PJD study
Substantial reduction of joint damage



TSS: Total Sharp Score; JSN: Joint Space Narrowing; ES: Erosion Score

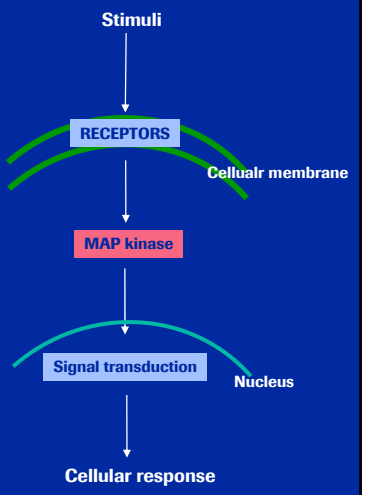
Actemra in RA
Summary and outlook

- Actemra monotherapy is effective in controlling:
  - signs and symptoms of RA (excellent ACR scores)
  - 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 excellent Japanese results
  - more than 4,000 patients to be enrolled
  - filing planned for 2007
- Actemra, through its novel mechanism of action, will soon become a new option for patients suffering from RA

R1503: p38 kinase inhibitor

First oral "anti-TNF" treatment

- **MAP kinases** are a group of serine/ threonine protein kinases that are activated in response to a variety of extracellular stimuli and mediate signal transduction for cellular inflammatory response
- **P38 kinase**
  - the newest member of MAP kinase family
  - it is activated in response to inflammatory cytokines and endotoxins
- **R1503 phase II**
  - started Q4'05
  - randomized, double-blind, placebo-controlled
  - dose-ranging
  - First data available mid-2007
- Filing planned in post 2009



Oncology – the main current growth driver

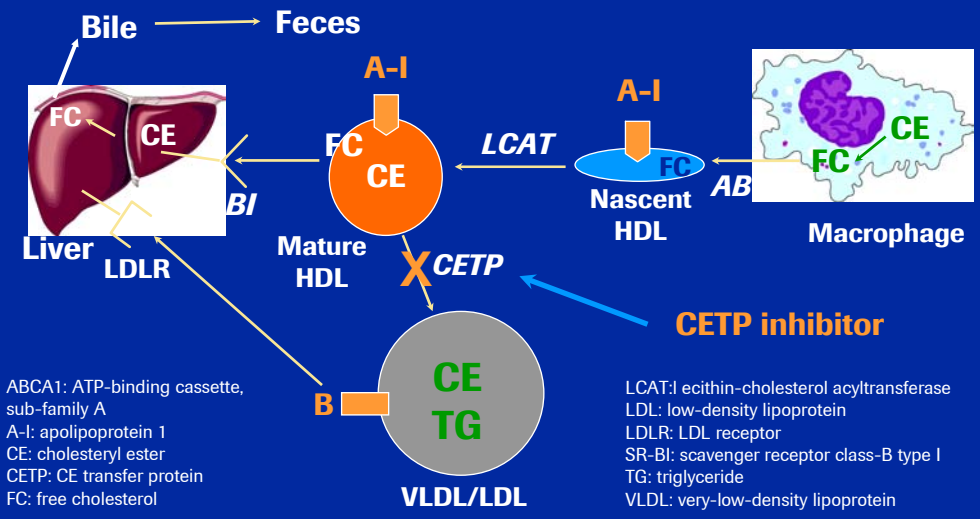
Rheumatoid arthritis – emerging disease area for growth

Metabolic diseases – therapeutic area for future growth

Summary

Q&A

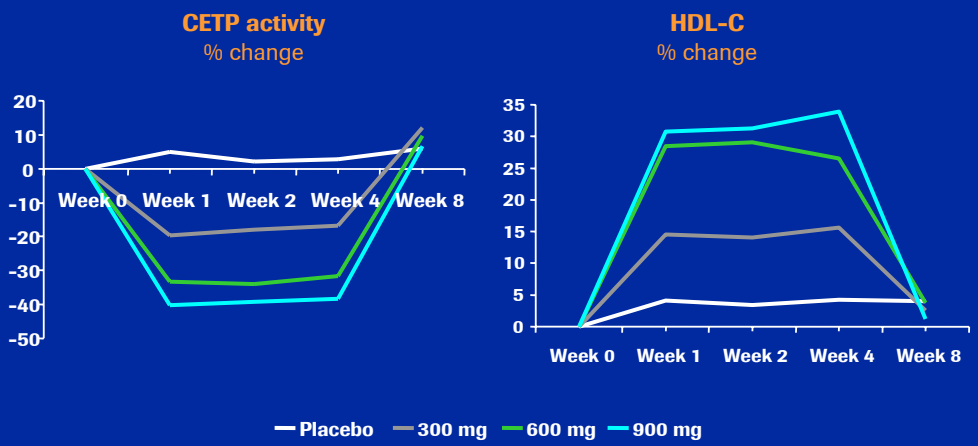
CETP inhibition as a novel strategy to raise HDL



ABCA1: ATP-binding cassette, sub-family A
A-I: apolipoprotein 1
CE: cholesteryl ester
CETP: CE transfer protein
FC: free cholesterol

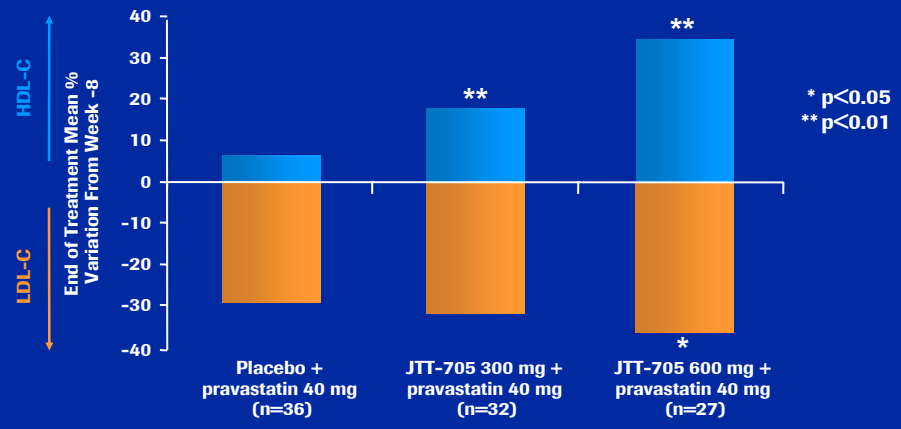
LCAT:l ecithin-cholesterol acyltransferase
LDL: low-density lipoprotein
LDLR: LDL receptor
SR-BI: scavenger receptor class-B type I
TG: triglyceride
VLDL: very-low-density lipoprotein

JTT-705/ R1658 (CETP inhibitor): Phase IIa
Monotherapy



de Grooth GJ et al. Circulation 2002;105:2159-65, phase II study in healthy subjects with mild hyperlipidemia (N=198); 0, 300, 600, 900 mg qd for 4 weeks

JTT-705/ R1658 (CETP inhibitor): Phase IIa
Combination with pravastatin



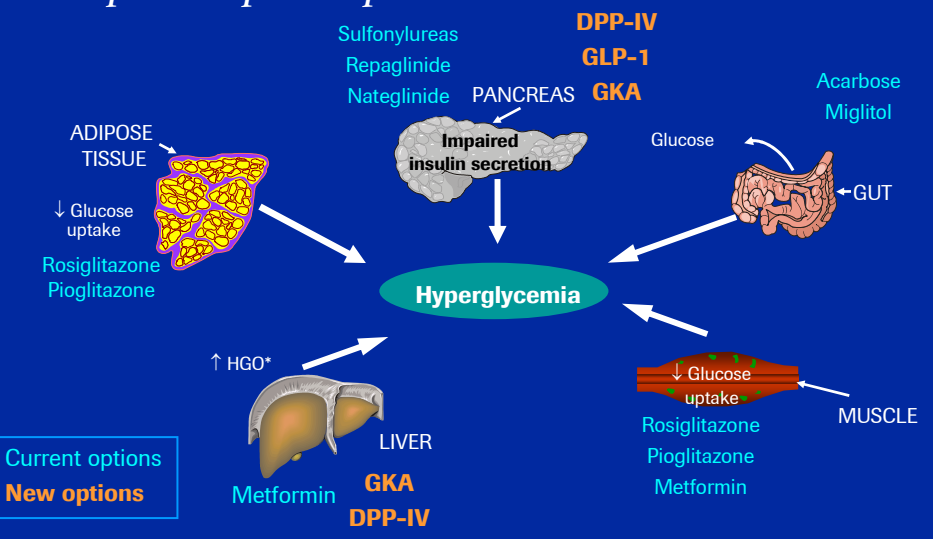
Pravastatin administered for 12 weeks; JTT-705 administered for the last 4 weeks

Kuivenhoven JA et al. Am J Cardiol 2005;95:1085-8, 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 (CETP inhibitor)
Summary and outlook

- Roche and Japan Tobacco signed agreement for development and commercialization 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, no increase in blood pressure observed
- 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

Type 2 Diabetes
Multiple therapeutic options



*HGO=hepatic glucose output.

BIM-51077/ R1583 (GLP-1): Partnered with Ipsen
Promising 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

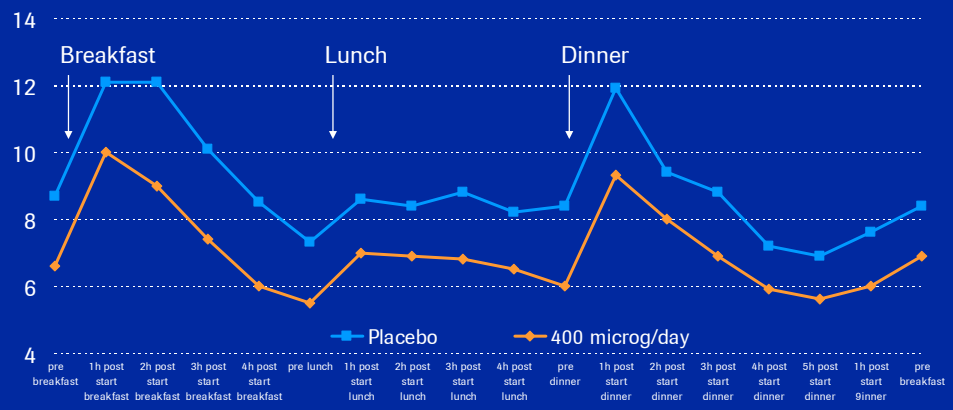
Sustained release formulation

- 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 (GLP-1)
Phase II 28 days continuous infusion

24h profile of blood glucose concentrations

Day 28, mean glucose concentration [mmol/L]



18 T2D patients treated with metformin, 12 active, 6 placebo, 28-day continuous subcutaneous infusion of BIM-51077 IRF

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

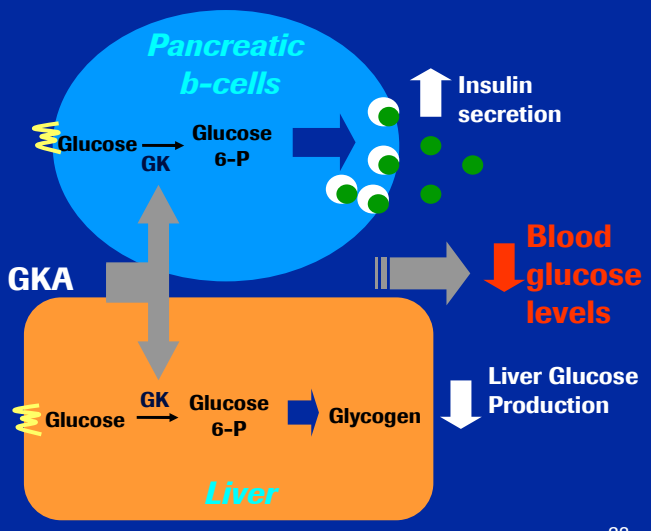
- Greater binding potency than native protein
- Extended metabolic half life (22-fold more stable in plasma)
- Sustained improvement in blood glucose control over days by continuous infusion
- Good safety profile, no antibodies against BIM-51077
- Significant and rapid effect on 24h blood glucose following 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
  - highly competitive environment
- R1438 (DPP IV inhibitor)
- Potentially best in class molecule
- 2 phase II ongoing
  - mono and combo with metformin
  - to complete end 2006/ early 2007
  - filing planned in 2009

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 targets 2 of the underlying pathologies in T2D
  - impaired insulin secretion
  - increased liver glucose production



R1440 (GKA)
Summary and outlook

- 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 advantages
  - oral
  - targets two underlying mechanisms of type II diabetes pathogenesis

Oncology – the main current growth driver

Rheumatoid arthritis – emerging disease area for growth

Metabolic diseases – therapeutic area for future growth

Summary

Q&A

Our objectives for 2006 – Pharmaceuticals

Announced for 2006

Major clinical data

Compound	Phase	Indication	Data	Status H1
Mircera (CERA)	III	Renal anemia (correction)	Final	✓
CellCept	III	Lupus nephritis (Induction phase)	Final	
Herceptin	III	mBC combo hormonal (TAnDEM)	Final	✓
Xeloda	III	mCRC 2nd line	Final	
Avastin	III	NSCLC 1st line (AVAIL)	Interim	✓
Avastin / Xeloda	III	mCRC 1st line combo extension	Final	✓
R1658	II	Dyslipidemia	Final	✓
R873	IIa	MED	Final	
Avastin / Tarceva	II	NSCLC 2nd line	Final	✓
R1594	II	RA	Final	✓

Filings

Compound	Indication	Status H1
Mircera (CERA)	Renal anemia	✓
Avastin	NSCLC 1st line	✓
Avastin	mBC 1st line	✓
Avastin	mCRC 1st line extension	
Herceptin	Adjuvant BC	✓
Herceptin	mBC combo hormonal	
Xeloda	mCRC 1st line combo	

Divisional sales growth

Double-digit growth in local currencies

barring unforeseen events

Summary

Building additional value propositions

- Oncology - on hands and further expansion
- Autoimmune diseases/ rheumatoid arthritis - in 'late stage' of development/ early launch
- Metabolic disease - a potential opportunity for future growth shaping up
- CNS - still in an early stage

Oncology – the main current growth driver

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Summary

Q&A

We Innovate Healthcare

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

Trial	Treatment	Sample Size	Endpoints
MTX-IR **SERENE**	MTX + placebo vs. MTX + MabThera 1g vs. MTX + MabThera 2g	495	Reduction in signs and symptoms
MTX naïve **(X-ray study)** **IMAGE**	MTX vs. MTX + MabThera 1g vs. MTX + MabThera 2g	852	Reduction in signs and symptoms Inhibition of structural joint damage Improvement in physical function
MTX-IR **Dose escalation** **MIRROR**	Rituximab 1g retx 1g vs. Rituximab 1g retx 2g vs. Rituximab 2g retx 2g	375	Effect of further courses and dose escalation

EU Filing 2008

Roche's phase III program for Actemra

Five trials ongoing

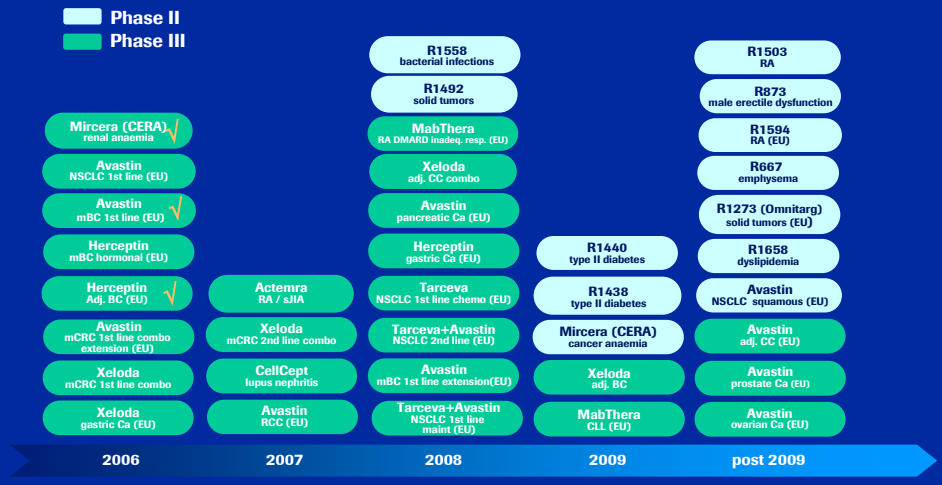
Treatment	Sample Size	Patient population	Endpoints
Actemra 4 mg + MTX Actemra 8mg + MTX MTX **OPTION**	630	MTX partial responders	ACR 20 response at Wk 24
Actemra 4 mg + MTX Actemra 8 mg + MTX MTX **LITHE**	1'170	MTX partial responders	ACR 20 at Wk 24 Sharp Score at Wk 52 Sharp Score at Wk 104 Physical function at Wk 104
Actemra 8 mg + DMARDs DMARDs **TOWARD**	1'200	DMARD partial responders	ACR 20 response at Wk 24
Actemra 4 mg + MTX Actemra 8 mg + MTX MTX **RADIATE**	570	Anti-TNFα failures	ACR 20 response at Wk24
Actemra 8 mg MTX **AMBITION**	550	MTX naive	ACR 20 response at Wk 24

Filing 2007

A rich and low risk Phase III pipeline
Keeping the high level of commitment

* Approved in July 2006
Status as of June 30, 2006

Major Roche managed projected submissions over the next years



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

phase 0 (14 NMEs)		phase I (21 NMEs + 3 AIs)		phase II (18 NMEs + 10 AIs)		phase III (2 NMEs + 34 AIs)		Registration (2 NMEs + 8 AIs)	
R1599	osteoarthritis	R1541	IBD	R1558	bacterial infections	R1569	Actemra RA	R744	Mircera renal anaemia
R1511	type 2 diabetes	R1295	RA	R1503	RA	CHU	ED-71 osteoporosis	CHU	Antevas subarach haemor
R1579	type 2 diabetes	R3421	AI / transplant	R1594	RA	R1569	Actemra sJIA	R597	Herceptin adj BC
R1646	OAB	R1439	type 2 diabetes	R1440	type 2 diabetes	R99	CellCept MG/PV	R105*	MabThera INHL maint relapse
R1663	anticoagulant	R1593	dyslipidemia	R1438	type 2 diabetes	R99	CellCept lupus nephritis	R105*	MabThera RA TNF nonresp
R641	Alzheimer's	R1664	dyslipidemia	R1658	dyslipidemia	R105	MabThera RA DMARD nonresp	R435	Avastin NSCLC 1st line
R1647	depression	R1450	Alzheimer's	R873	MED	R105	MabThera CLL 1st line	R435	Avastin mBC combo Taxol 1st
R1551	schizophrenia	R1678	schizophrenia	R1273	ovarian cancer	R105	MabThera CLL relapsed	R1415	Tarceva pancreatic ca
R7118	schizophrenia	R7090	anxiety	R1492	solid tumors	R105	MabThera iNHL maint 1st line	CHU	Epogin cancer anaemia
R7159	NHL	R547	solid tumors	R667	emphysema	R1415	Tarceva NSCLC 1st line	CHU	Sigmart acute heart fail
R1206	HIV	R1454	solid tumors	R411	asthma	R1415+R435	T+A NSCLC 2nd line		
R7025	HCV	R1507	solid tumors	CHU	gastroparesis	R1415+R435	T+A NSCLC 1st line maint		
R7128	HCV	R1530	solid tumors	CHU	osteoporosis	R340	Xeloda mCRC combo 1st line		
CHU	solid tumors	R1645	solid tumors	CHU	post-hepatectomy	R340	Xeloda mCRC combo 2nd line		
		R1656	HCV	GEN	diabetic foot ulcers	R340	Xeloda adj CC combo		
		R1626	HCV	ISO	renal transplant	R340	Xeloda adj BC		
		GEN	RA / Sjögrens syndrome	IPS**	type 2 diabetes	R340	Xeloda gastric cancer		
		GEN	basal cell carcinoma	ARQ	solid tumors	R435	Avastin adj CC		
		GEN	cancer	R744	Mircera cancer anaemia	R435	Avastin mBC combo Taxotere 1st		
		GEN	mBC	R435	Avastin NSCLC squamous	R435	Avastin mBC combo nonTaxanes 1st		
		MEM	Alzheimer's	R435	Avastin NSCLC mCNS treat	R435	Avastin pancreatic ca		
		R127	Valganciclovir ulcerat colitis	R1415	Tarceva glioblastoma	R435	Avastin RCC		
		R1594	NHL	R1273	mBC	R435	Avastin prostate ca		
		R35	Daclizumab transpl maint	R35	Daclizumab asthma	R435	Avastin ovarian cancer		
				GEN	Lucentis diabetic macular edema	R435	Avastin mCRC 1st line ext		
				GEN	Avastin adj BC HER2-	R597	Herceptin mBC combo		
				GEN	Avastin glioblastoma	R597	Herceptin gastric ca		
				GEN	MabThera RRMS	R127	Valcyte CMV ext		
						GEN	Xolair pediatric asthma		
						GEN	Avastin GIST		
						GEN	Avastin adj rectal cancer		
						GEN	Avastin mBC 2nd line		
						GEN	MabThera lupus nephritis		
						GEN	MabThera PPMS		
						GEN	MabThera ANCA ass vascul		
						GEN	MabThera SLE		

* EU approval July 2006

** Opted-in July 2006

NME (New Molecular Entity)
- R Roche managed projects
- A Participations
- A Opt-in Opportunities

AI (Additional Indication)
- R Roche managed projects
- A Participations
- A Opt-in Opportunities

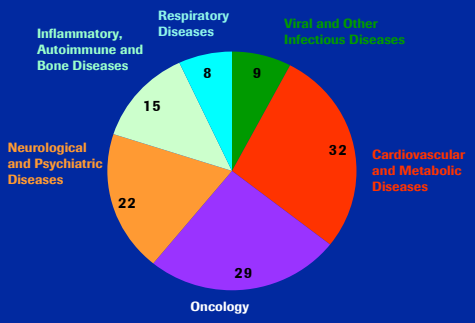
CHU Chugai
GEN Genentech
IPS Ipsen
ISO Isotechnika
MEM Memory
ARQ ArQule

Status as of June 30, 2006

Roche managed R&D pipeline – overview

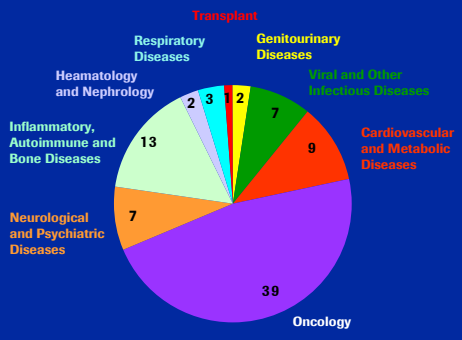
Projects by Therapeutic Area

Research



115 projects

Development



83 projects

Status as of June 30, 2006