

Roche Pharma Development

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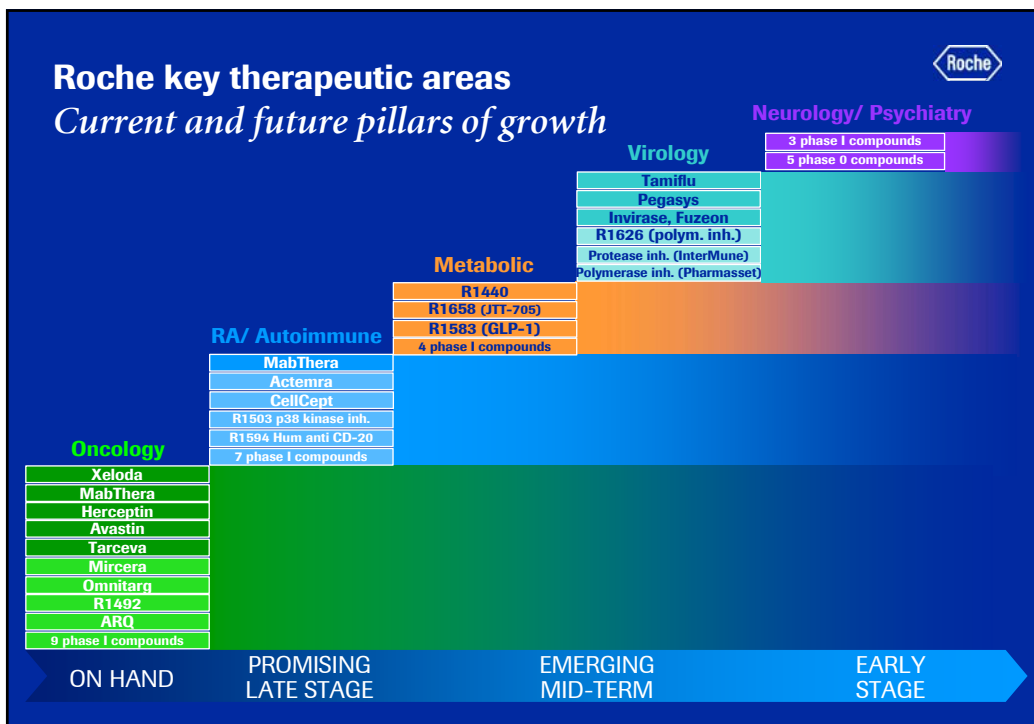
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Oncology – main current growth driver

Rheumatoid arthritis – emerging disease area for growth

Anemia – expanding a strong presence

Metabolic diseases – therapeutic area for future growth

HCV – expanding current portfolio

Summary

Q&A

4

Oncology: A rich phase III pipeline



Targeting main tumor types and use in early intervention

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

5

Our commitment to develop Avastin in metastatic breast cancer



| | HER 2 +ve | HER 2 -ve | | | |
|--------------------|---------------------------------|---|---|---|---|
| Study | AVEREL | E2100 | AVADO | RIBBON-1 | RIBBON-2 |
| | phase III | phase III | phase III | phase III | phase III |
| Patient population | 1 st line | 1 st line | 1 st line | 1 st line | 2 nd line |
| Treatment regimen | Herceptin + Docetaxel ± Avastin | Paclitaxel ± Avastin | Taxotere ± Avastin 7.5mg/Kg or 15mg/Kg both q3weeks | Anthracyclines based or Xeloda or Taxanes based ± Avastin | CT (taxane based, Gemcitabine, Vinorelbine, Capecitabine) ± Avastin |
| No of patients | 320 | 722 | 705 | 900-1050 | 630 |
| Status | Started in Sep '06 | Completed - superior PFS and improved OS with addition of Avastin | Ex US Started Q1'06 | Started Q4'05 | Started Q1'06 |

6

Combining targeted therapies without chemo

Promising efficacy and favorable safety profile

| | Median PFS | Alive at 6 months | Alive at 12 months |
|---|-----------------------|-------------------|--------------------|
| NSCLC 2 nd line, after platinum-based CT (n=120) → Avastin + Tarceva | 4.4 months (HR= 0.72) | 78 % | 57 % |
| NSCLC 2 nd line, after platinum-based CT (n=120) → Avastin + CT (pemetrexed or docetaxel) | 4.8 months (HR= 0.66) | 72 % | 54 % |
| NSCLC 2 nd line, after platinum-based CT (n=120) → CT (pemetrexed or docetaxel) | 3.0 months | 62 % | 35 % |

- Exploratory phase II trial
- Primary endpoint: PFS vs. chemotherapy alone
- No unexpected side effects

Presented at ASCO June'06

Presented at EORTC Nov'06

Phase III Tarceva + Avastin in 2nd line NSCLC ongoing, data available 2008

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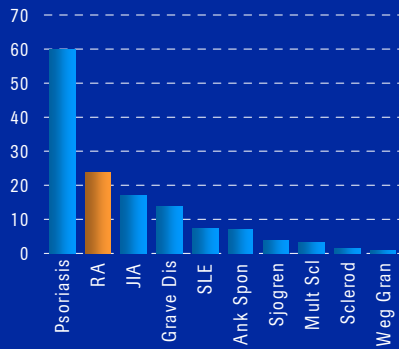
Q&A

Autoimmune diseases

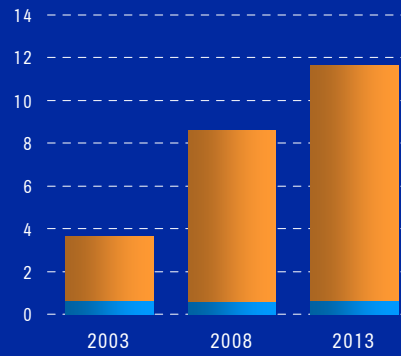


Among the leading causes of death in young and middle aged women

Global incidence autoimmune diseases
Per 10,000 Patient years (PY)



Global sales to treat RA (\$bn)¹



**Autoimmune diseases: female predominance (~65%)
Affects ~5 to 8% of the population**

¹ Source : Decision Resources, March 2005

Roche in autoimmune diseases



Building a new therapeutic franchise

MabThera - RA

Actemra - RA, sJIA

CellCept - Lupus Nephritis

MabThera - LN, PPMS, ANCA ass. vasculitis, SLE

Ocrelizumab - RA

R1503 (p38 kinase inhibitor) - RA

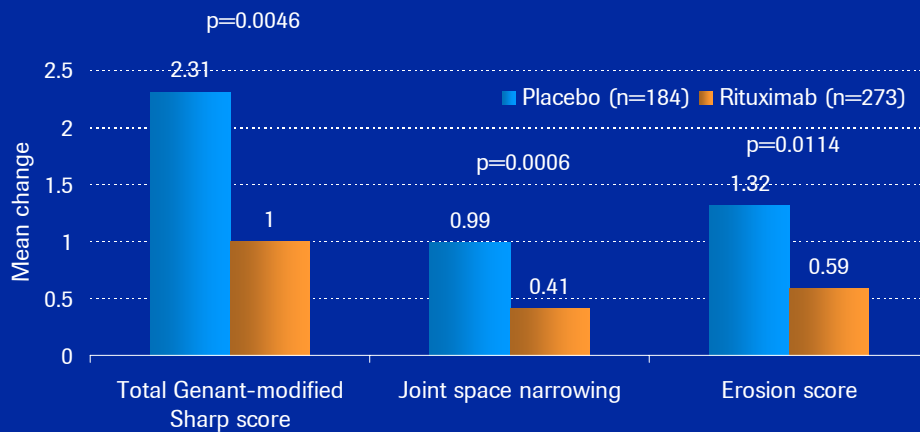
MabThera - RRMS

Phase 1 - 7 compounds in development



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

Significant inhibition of radiographic progression at Week 56



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

11

MabThera/ Rituxan

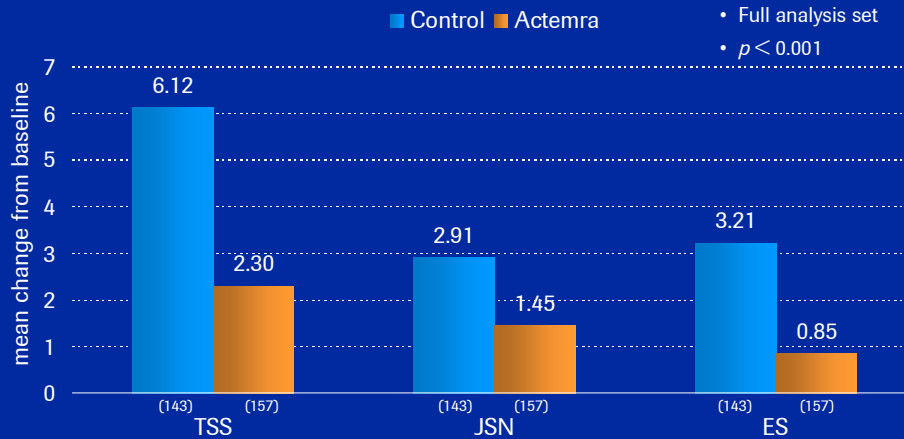
Summary and outlook

- REFLEX study provides first indication that a **B cell-targeted therapy can inhibit radiographic progression**
 - the only compound to show 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
 - enrollment of more than 1,700 patients ongoing
 - EU filing planned in 2008

12

Actemra in RA: SAMURAI, PJD study

Substantial reduction of joint damage



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

13

Actemra in RA

Summary and outlook



- Actemra monotherapy is effective in controlling
 - signs and symptoms of RA (excellent ACR scores)
 - progression of structural damage
- Effectiveness sustained over time
- Generally well tolerated
- 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

14

R1594 (Ocrelizumab): Phase I/II ACTION

Phase III to start in 2007

Study design

- 237 patients with moderate-severe RA
- Phase I/II dose-escalation: MTX + ocrelizumab (IV days 1 and 15)
- Primary endpoint: safety and tolerability

Results

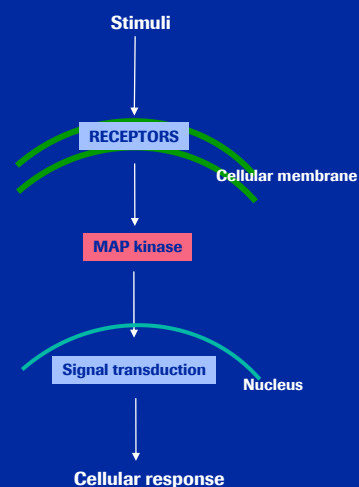
- **Well tolerated at all doses**
 - most frequent AEs: infusion-associated grade 1/2 headaches, nausea, chills, pyrexia, and dizziness
 - rate of SAEs and infection-related SAEs was similar in the groups
 - low immunogenicity at doses 200mg and higher (HAHA)
- **Clinical activity at all doses**

15

R1503: p38 kinase inhibitor

First oral “anti-TNF” treatment

- **P38 kinase**
 - the newest member of MAP kinase family
 - it is activated in response to inflammatory cytokines and endotoxins
- **R1503 phase II**
 - randomized, double-blind, placebo-controlled
 - dose-ranging
 - **First data available mid-2007**
- **Filing planned in post 2009**



16

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Q&A

Chronic Kidney Disease (CKD)

A global problem

Prevalence / Incidence

> 500 million people worldwide

~ 1 in 10 of the general population have some degree of CKD¹

~ 250,000 new patients are diagnosed with CKD each year²

High medical need

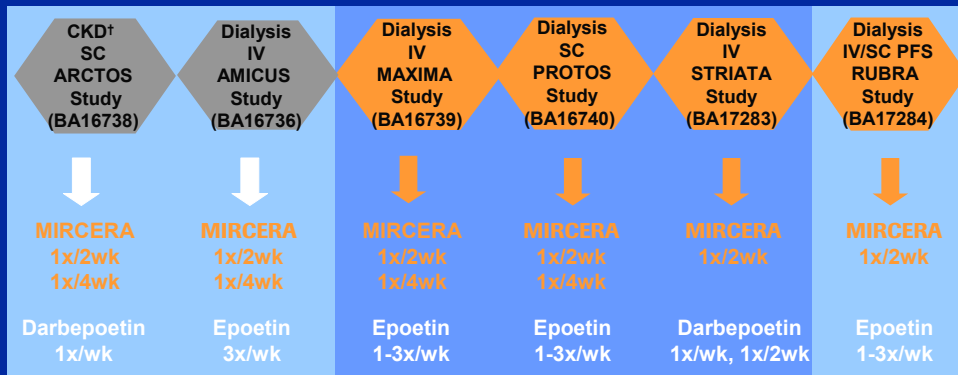
- 2/3 of patients are not maintained within target Hb range
- 9 out of 10 patients experience Hb “cycling”
- dosing - majority of patients still receive TIW (3x/wk) or QW (1x/wk) dosing

Overview of MIRCERA phase III trials

A comprehensive renal clinical program - 2700 patients in 29 countries

ESA-naïve patients

ESA-treated patients



*Patients with CKD not on dialysis

Schedule for conversion

Presented at ERA-EDTA 2006

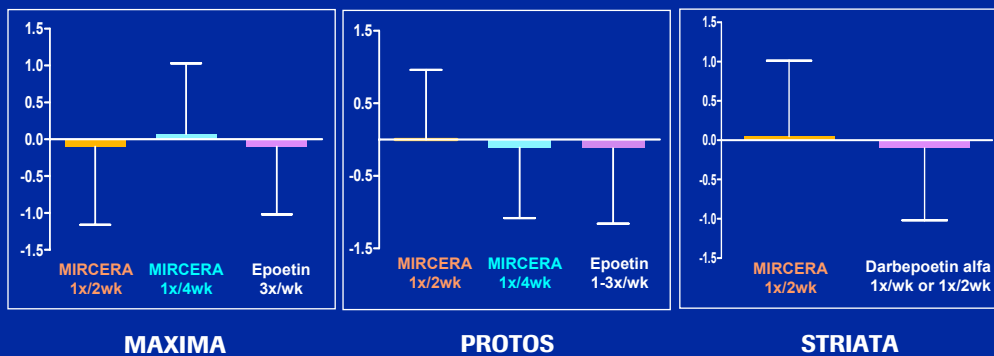
Presented at ASN 2006

19

Phase III in maintenance: Primary endpoint met

No change in mean Hb levels

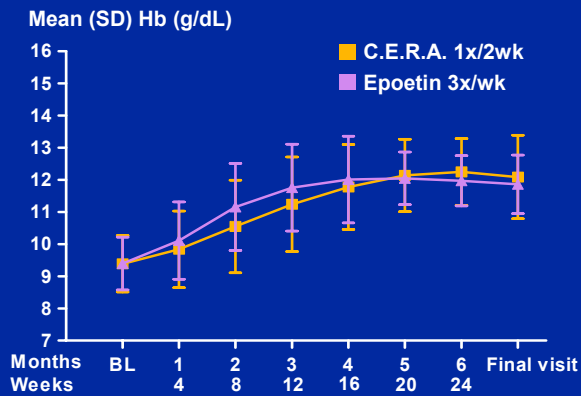
Mean (SD) Hb change between baseline and evaluation periods (g/dL)



20

Phase III in correction: Primary endpoint met
Smooth and steady Hb increase with a high response rate

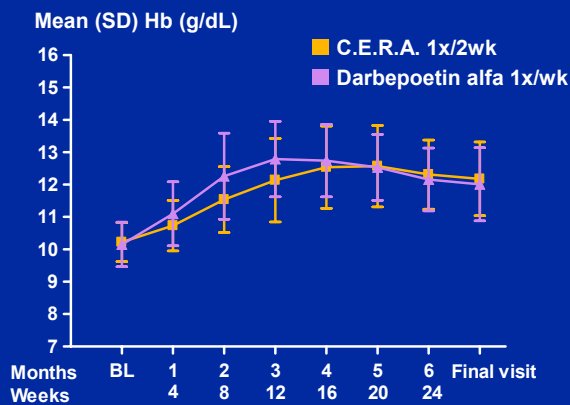
AMICUS (iv in dialysis)



| | Response rate (%) | 95% CI |
|-----------------|-------------------|-----------|
| C.E.R.A. 1x/2wk | 93.3 | 87.7-96.9 |
| Epoetin 3x/wk | 91.3 | 79.2-97.6 |

Phase III in correction: Primary endpoint met
Smooth and steady Hb increase with a high response rate

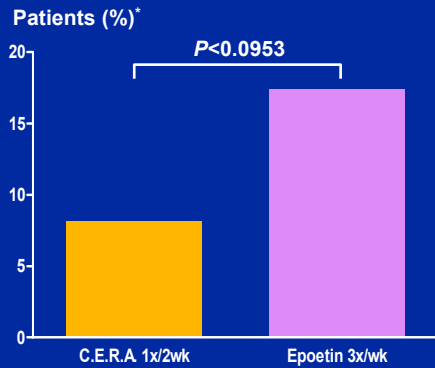
ARCTOS (sc in pre-dialysis)



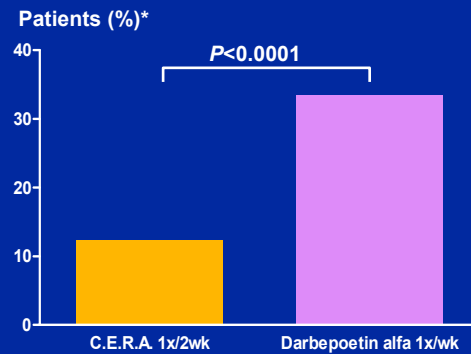
| | Response rate (%) | 95% CI |
|-------------------------|-------------------|-----------|
| C.E.R.A. 1x/2wk | 97.5 | 93.8-99.3 |
| Darbepoetin alpha 1x/wk | 96.3 | 92.1-98.6 |

Fewer patients exceed Hb 13 g/dL with Mircera *Seen in both phase III correction trials*

AMICUS (iv in dialysis)



ARCTOS (sc in pre-dialysis)



*Patients with ≥ 1 Hb value > 13 g/dL during first 8 weeks

23

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24

Roche in metabolic/ cardiovascular diseases
Major decision points within the near future

R1583 (GLP-1) – Type II Diabetes

R1440 (GKA) – Type II Diabetes

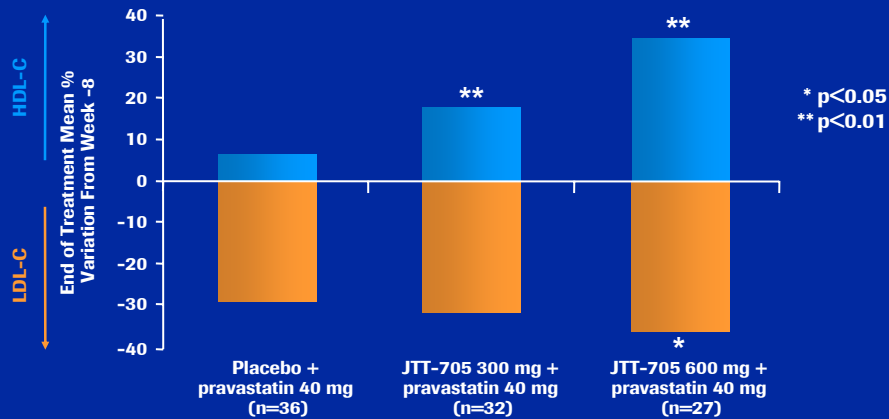
R1658 (CETP inh) – Dyslipidemia

Phase I - 4 compounds in development

Phase 0 - 4 compounds in development



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

- Benefits of CETP inhibition in hyperlipidemia/ dyslipidemia confirmed
- **No increase in blood pressure**
- Phase II in dyslipidemia (combination with pravastatin)
 - primary endpoint: percentage and absolute change from baseline at Week 12 in HDL-C level (efficacy)
 - **encouraging efficacy data with once daily administration**
 - safety trial ongoing
- Go/ no go decision for phase III in 2007

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)



Summary and outlook

- Extended metabolic half life (22-fold more stable in plasma)
- **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**

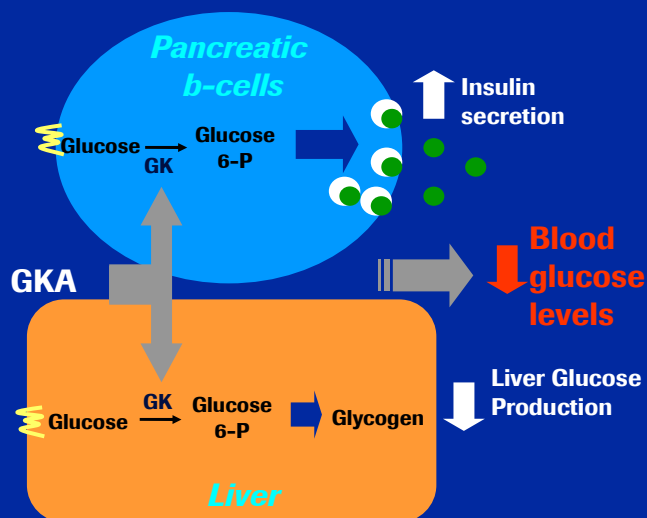
29

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



30

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)
 - first data in 2007
 - filing planned in 2009
- **Main differentiators**
 - oral
 - targets two underlying pathogenic mechanisms of T2D

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Roche in Hepatitis C

Expanding current portfolio

R1626 (polymerase inhibitor)

- Phase I full data presented at AASLD '06
- Phase II initiated October '06
- FDA fast track status granted

R1656/R7128 Pharmasset (polymerase inhibitors)

- Phase I ongoing

R7227 InterMune (protease inhibitor)

- Phase I to start by end '06

R7025 Maxygen (peg. interferon)

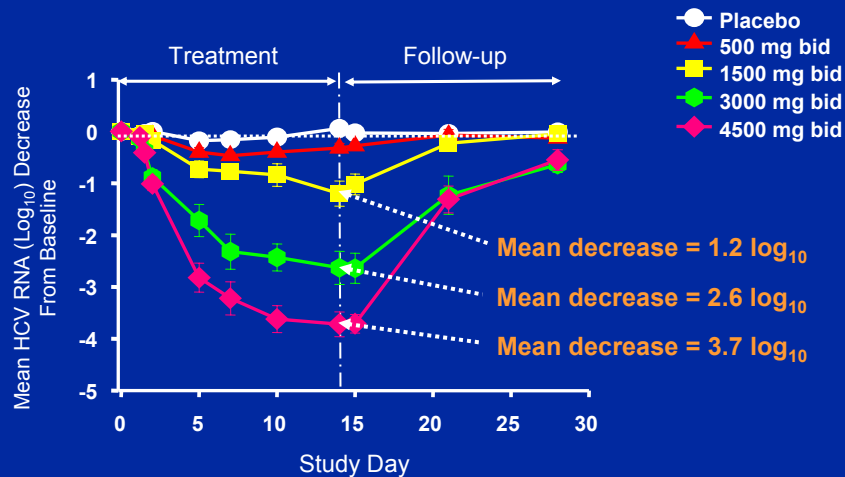
- Phase I initiated in November '06



33

R1626: Phase I data

Robust antiviral effect



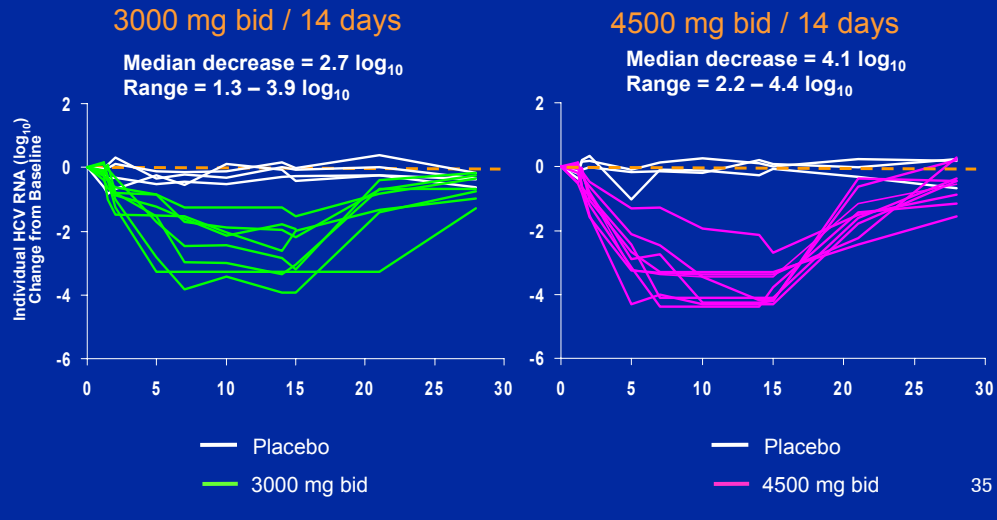
– 8/9 BQL (<600 IU/mL) and 5/9 PCR negative (<50 IU/mL) at 4500 mg bid dose

34

R1626: Phase I data



Consistent drop in viral load across individual patients



R1626: Phase I data



Summary

- Greatest viral load reductions seen in this class
 - robust antiviral effect with mean viral load reductions of 1.2 – 3.7 log₁₀ following 14 days of monotherapy
- No viral resistance observed
- Good tolerability
 - Increasing adverse events at higher dose levels
 - Reversible mild to moderate hematologic changes were treatment- and time-related

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2006/7: Further strong newsflow expected

Oncology: 4 phase III, 2 phase II, 3 phase I

Avastin

- EU filing mCRC label extension
- Phase III data available AVOREN, CALGB 90206 (RCC)
- Final analysis AVAIL (NSCLC)
- Recruitment completed AVANT (adj. CC), AVADO (mBC)
- Start of phase III in adj. NSCLC, ovarian Ca

Xeloda

- Global filing mCRC label extension
- Final analysis mCRC 2nd line

MabThera

- Recruitment completed PRIMA (iNHL 1st line maint.)

Omnitarg

- Phase II data available

R1492/R1584 (EpoD)

- Go/ No go decision for phase III and II

R547 (CDK-inh)

- Go/ No go decision for phase II

R1530 (MAI)

- Go/ No go decision for phase II

Anemia

Mircera

- Phase III correction data to be presented at ASN' 06

Autoimmune diseases: 6 phase III, 1 phase II

Actemra

- Final analysis of 4 phase III trials (RA)
- Recruitment completed LITHE (RA)

MabThera

- Recruitment completed SERENE and SUNRISE (RA)
- Phase II data (HERMES) in RRMS to be presented
- Go/ No go decision for phase III in RRMS

CellCept

- Final analysis phase III Lupus Nephritis
- Final analysis phase III Myasthenia Gravis

Ocrelizumab

- Phase II (ACTION) to be presented at ACR '06
- Start of phase III in RA

R1503 (p38 kinase inh)

- First phase II data available

Metabolic/ Cardiovascular diseases: 2 phase II

R1440 (GKA)

- First phase II data available

R1658 (CETP inh)

- Phase II completed
- Go/ No go decision for phase III

2006/7: Further strong newsflow expected

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Xeloda

- Global filing mCR
- Final analysis mCR

MabThera

- Recruitment completed

Omnitarg

- Phase II data available

R1492/R1584 (Epo)

- Go/ No go decision

R547 (CDK-inh)

- Go/ No go decision for phase II

R1530 (MAI)

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- Phase II data (HERMES) in RRMS to be presented at ACR '06

To be completed until mid '07:
10 phase III projects
5 phase II projects

- First phase II data available

Metabolic/ Cardiovascular diseases: 2 phase II

R1440 (GKA)

- First phase II data available

R1658 (CETP inh)

- Phase II completed
- Go/ No go decision for phase III

Summary

Building additional value propositions

- **Oncology** – worldwide leadership and continue to expand
- **Autoimmune diseases/ rheumatoid arthritis** – an emerging new growth area in late development stage – early launch
- **Anemia** – filed globally/ preparing for launch
- **Metabolic disease** – a potential opportunity for future growth shaping up
- **HCV** – new generation of drugs to be combined with Pegasys
- **CNS** – an attractive early portfolio

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Anemia –

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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-TNF α failures | ACR 20 response at Wk24 |
| Actemra 8 mg MTX AMBITION | 550 | MTX naive | ACR 20 response at Wk 24 |

Filing 2007

45

Actemra in RA

Japanese phase III results



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

46