Development at Roche

Participating in and driving the paradigm shift

Jean-Jacques Garaud, MD

Global Head Pharma Development, Chief Medical Officer

F.Hoffmann-La Roche Ltd

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

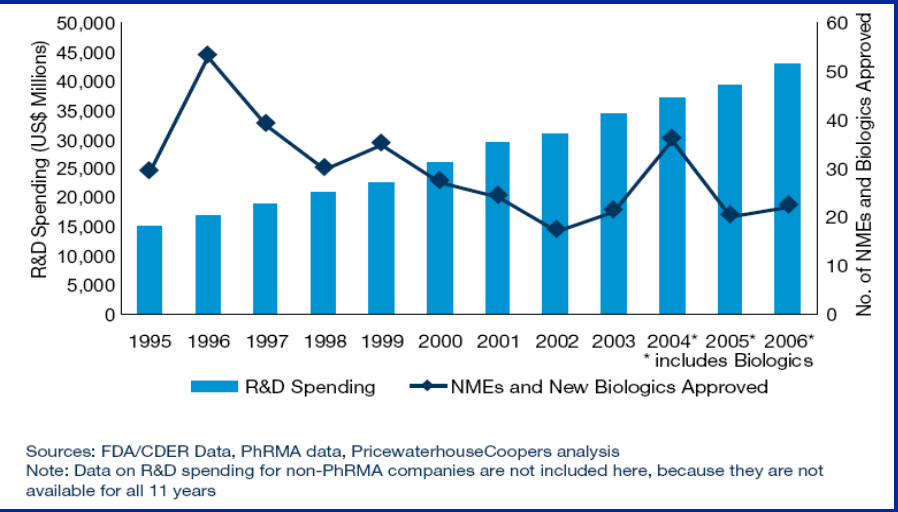
Our new R&D model: Paradigms changes

Franchises and assets

Summary

Decreasing R&D productivity

Need for new approaches to reverse the trend

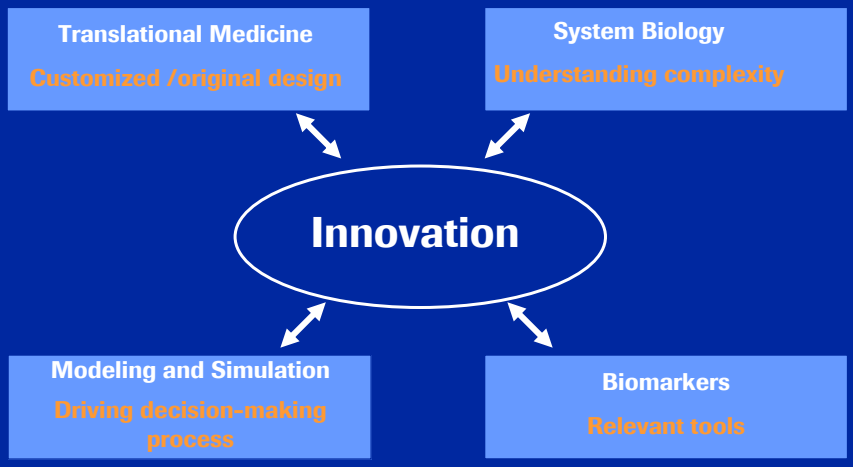


Sources: FDA/CDER Data, PhRMA data, PricewaterhouseCoopers analysis
Note: Data on R&D spending for non-PhRMA companies are not included here, because they are not available for all 11 years

Source: Price Waterhouse Coopers; Pharma 2020

New R&D model

Innovation truly at its core



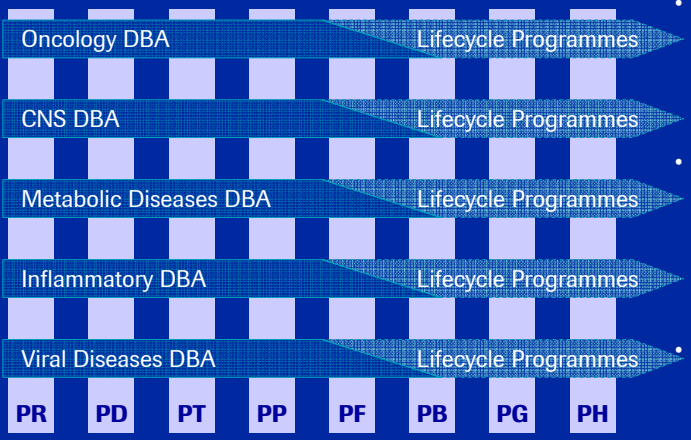
Creating New Differentiated Medicines

Achieved in a sustained fashion

- Informed decisions based on **deep knowledge of target and disease biology**:
  - Biomarkers
  - Importance of focus
- Encourage teams to take on non-chartered territories and **take risks**:
  - Innovation does not come from well established pathways
- Create interface between R&D that allows **collaborative, multi-disciplinary work**
- Leverage the **new methodologies**

New R&D Model

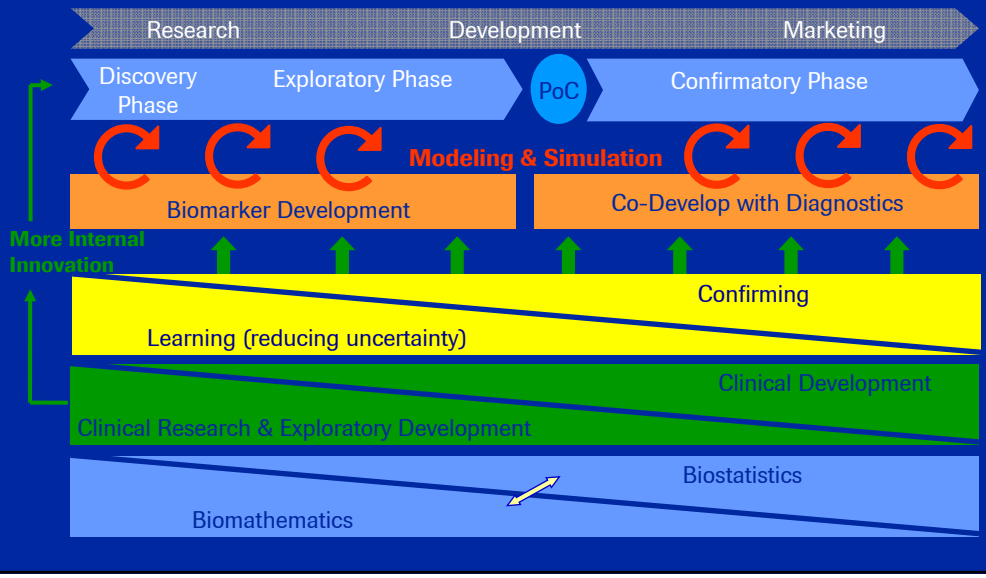
Cross - functional, translational, differentiated



- Integrate exploratory development expertise in cross-functional projects
- Deliver translational medicine approaches to select high-quality compounds for full development
- Apply and implement better-profiled and differentiated molecules in late-stage development

Development does never stop

Continuous with integration of biomarkers across development



Roche

Our new R&D model: Paradigms changes

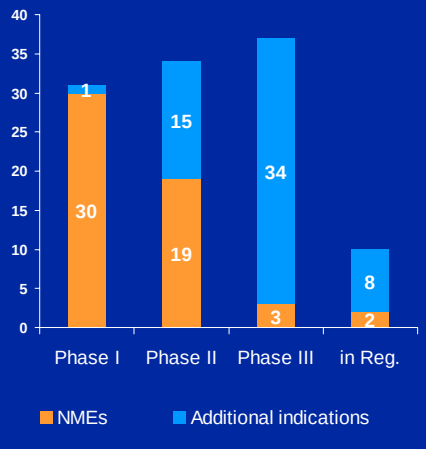
Franchises and assets

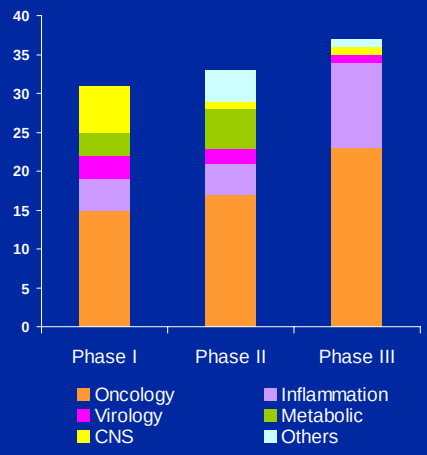
Summary

Roche

Pipeline: 54 NMEs and 58 additional indications

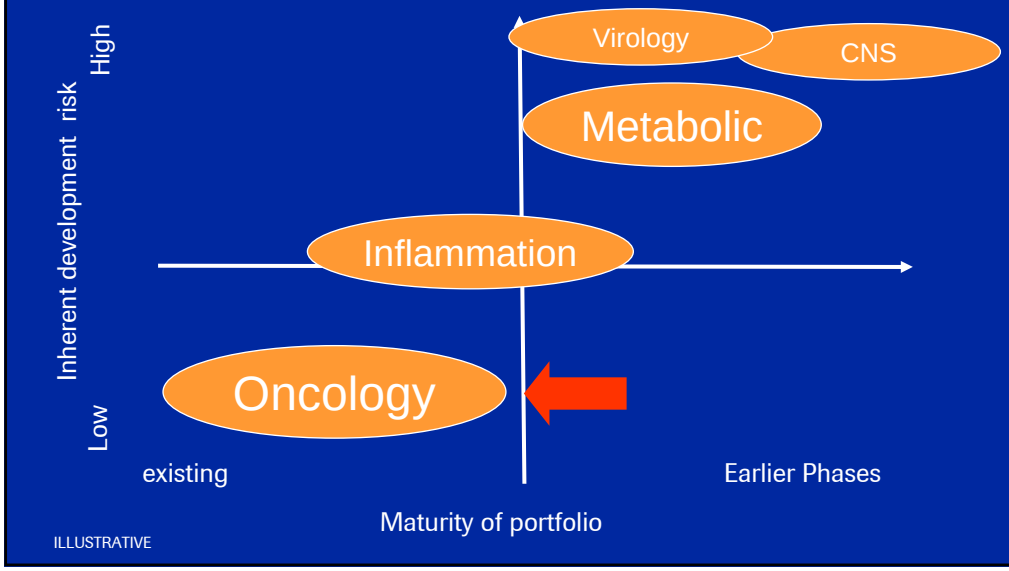
Staying strong in oncology and diversifying into new areas





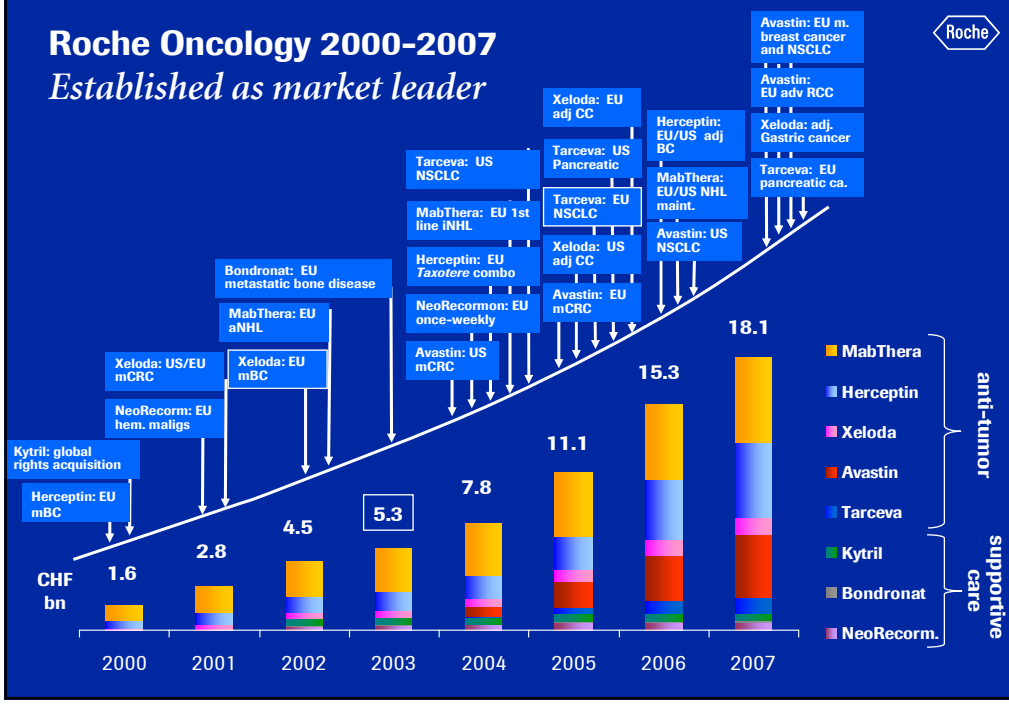
Key drivers for long term development in place

Develop the short term drivers while not 'leaving ' the others



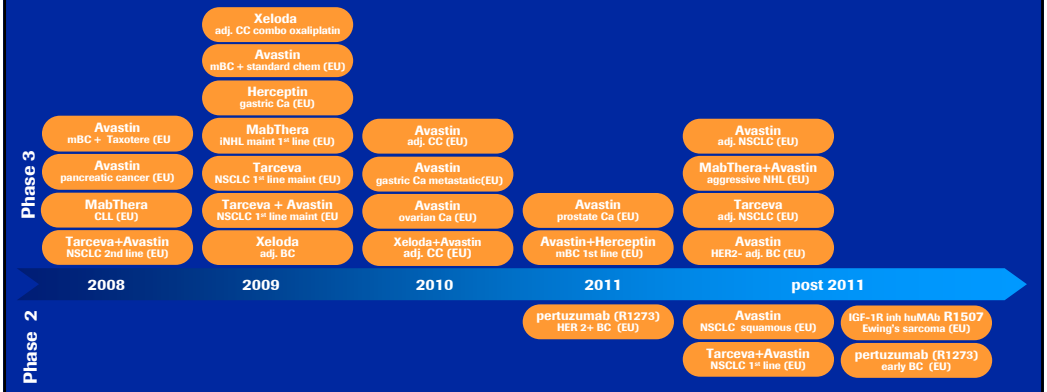
Roche Oncology 2000-2007

Established as market leader



Projected Oncology Submissions (Roche-Managed)

Over the coming years



Status as of December 31, 2007 Unless stated otherwise, submissions will occur in US and EU

Avastin still early in its journey

Realising full potential across tumour types

Tumour	Early/adjuvant (Potential for cure)	Advanced/metastatic (Extending life)	
		1st-line of treatment	2nd-line of treatment
Colon/ rectal	**Phase III** (AVANT, NSABP C-08, E5202, E5204)	✓ **Launched** [EU, US, JP; broad label in 1st and subsequent lines]	
Lung (NSCLC)	**Phase III** (E1505)	✓ **Launched** [EU majority of chemos, US carboplatin/paclitaxel]	**Phase III** (BETA Lung w/Tarceva)
Breast (HER2-)	**Phase III** (BEATRICE, E5103)	✓ **Launched** [EU paclitaxel] **Phase III** (AVADO, RIBBON-1)	**Phase III** (RIBBON-2, incl. w/Xeloda)
Breast (HER2+)	**Phase III** (BETH w/Herceptin)	**Phase III** (AVEREL w/Herceptin)	–
Kidney (RCC)	–	✓ **Launched** [EU; with interferon]	

Avastin also trialed in gastric, ovarian, prostate, aNHL, and brain (GBM)

(Trial names) [Approval status]. More trials are ongoing than listed above.

Attacking the HER2 pathway from multiple angles

Pertuzumab moving forward, Trastuzumab-DM1 in-licensed

	Herceptin	Pertuzumab	Trastuzumab-DM1
Mechanism	Specifically targeting HER2 Inhibits HER2-mediated signalling	First in class HER dimerization inhibitor Inhibits multiple HER-mediated pathways	Binds to HER2 and delivers intracellularly a potent cytotoxic agent in a targeted manner
Phase of development	Approved for adjuvant and mBC (HER2+)	Phase III CLEOPATRA FPI Q1 2008	Phase II FPI Q3 2007
Efficacy data	Survival benefit In adjuvant and metastatic HER2+ BC	18% response rate 39% clinical benefit rate	Promising phase I data at ASCO 2007
Newsflow	Unprecedented benefit – standard of care	Phase II final results in 2008	Partnered with Genentech

Examples of new market opportunities

Trastuzumab-DM1- *Very promising early data* *(Phase 1 data)*

(24 pts evaluated, - 6 objective responses, 4 responses on-going at the last data cut-off; the longest has persisted over 8 months- No unexpected cardiotoxicity so far

Moved into Phase II

3rd generation Anti-CD20s

Acquisition of Glycart paying off

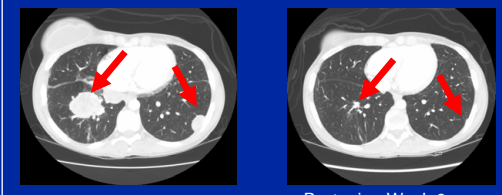
Increased CD20 binding and apoptosis

Increased ADCC; Reduced CDC

Moving into Phase II soon

IGF1-R Inhibitor – Impressive early results

Eligibility as multi-tumor compound?



Restaging Week 6

Unique Features- Selective to IGF pathway which is a key factor in tumor growth

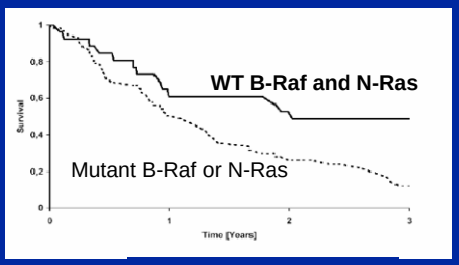
Drivers for Value – IGF pathway linked to many tumor types

Moved into Phase II

ADCC= (antibody dependent cell-mediated cytotoxicity); CDC= (complement dependent cytotoxicity)

Tailoring Early Clinical Trials: Example Prospective Patient Selection and Co-development of Pharmacodiagnostics

- About 15% of all human cancers have B-Raf mutations. ^{V600E}BRAF is causally involved in tumor growth and maintenance and is associated with worse prognosis.
- The efficacy of a BRAF inhibitor is assessed in Phase I in V600E-bearing tumors, including melanoma and CRC patients.
- Development of a pharmacodiagnostic assay for BRAF V600E mutation for Phase I, essential to allow prospective selection of patients for the trial.



Cancer Res 2006; 66: (2). January 15, 2006

Houben et al. Journal of Carcinogenesis, 2004

The future: Combination of targeted therapies
Roche in lead

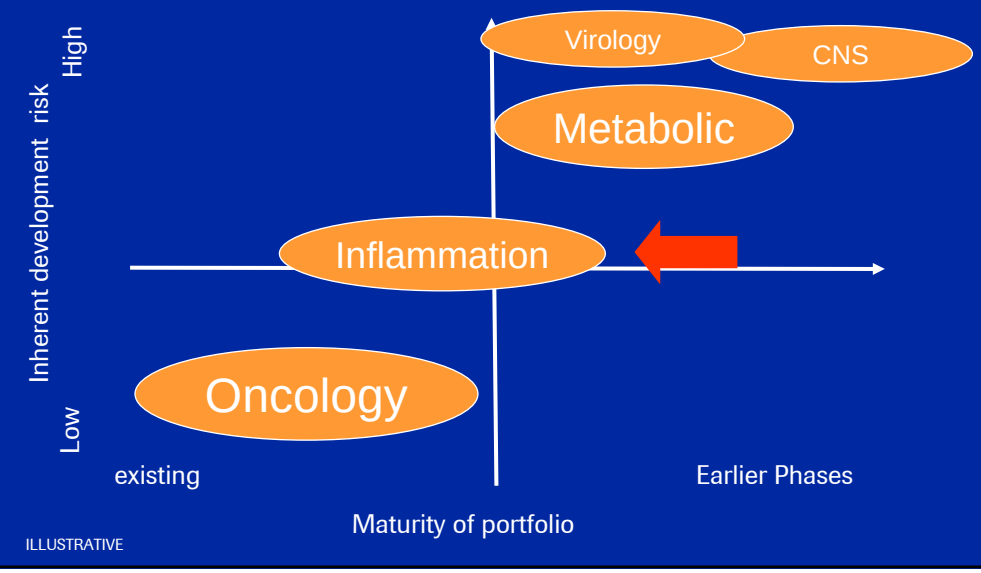
	NSCLC			Breast Cancer				Pancreatic
Study	ATLAS (Phase III)	BETALung (Phase III)	Phase II	AVEREL (Phase III)	Pegram (Phase II)	Phase III	Phase II	AVITA (Phase III)
Patient population	1st line maintenance non-squam.	2nd line	2nd line	1st line	1st line	Adjuvant	2nd line	1st line
Treatment regimen	CT + Avastin -> Avastin ± Tarceva	Tarceva ± Avastin	Avastin + Tarceva vs. Avastin + CT vs. CT	Herceptin + Taxotere ± Avastin	Herceptin + Avastin	Herceptin + Avastin tbd	Herceptin + Omnitarg	Gemcita-bine/ Tarceva ± Avastin
Status	Started Q4'05	Started Q2'05	Presented ASCO'06 SABC '06	Started Q3 '06	Presented SABC '06	Planned	Ongoing	Started H1'06

Potential patient benefits
- higher efficacy
- individualized treatment
- better tolerability

Roche setting the standard of care in combined targeted therapies

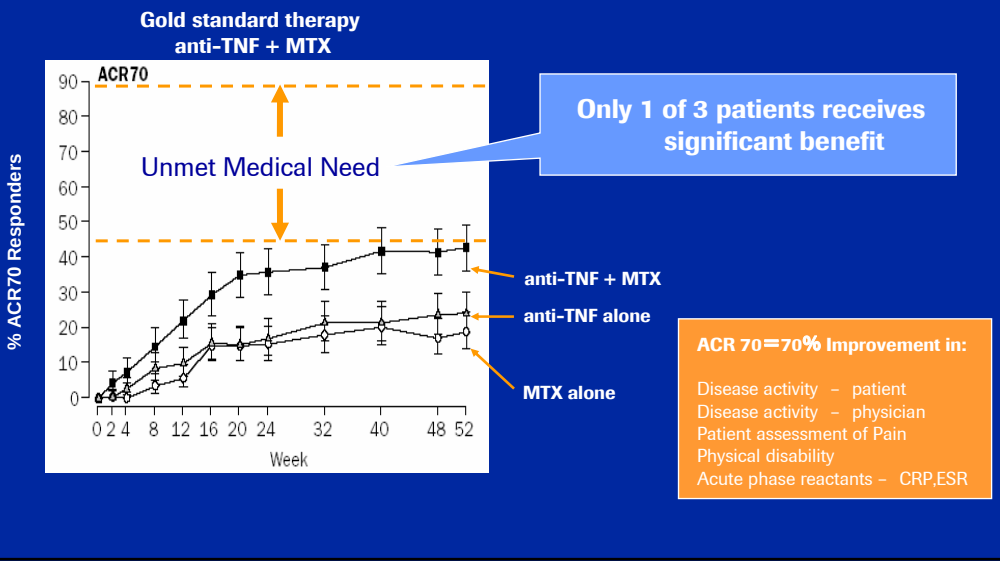
Key drivers for long term development in place

Develop the short term drivers while not 'leaving ' the others



ILLUSTRATIVE

Rheumatoid Arthritis: Not all patients respond to current therapy



Actemra

Potential to become a significant new RA treatment

First-in-class agent

- Humanized monoclonal antibody blocking the activity of IL-6 via inhibition of the IL-6 receptor
- Conclusions from phase III Jap trials
  - Impressive efficacy in DMARD inadequate responders
  - Effective as monotherapy
  - Well tolerated

Approved in Japan in April 2008

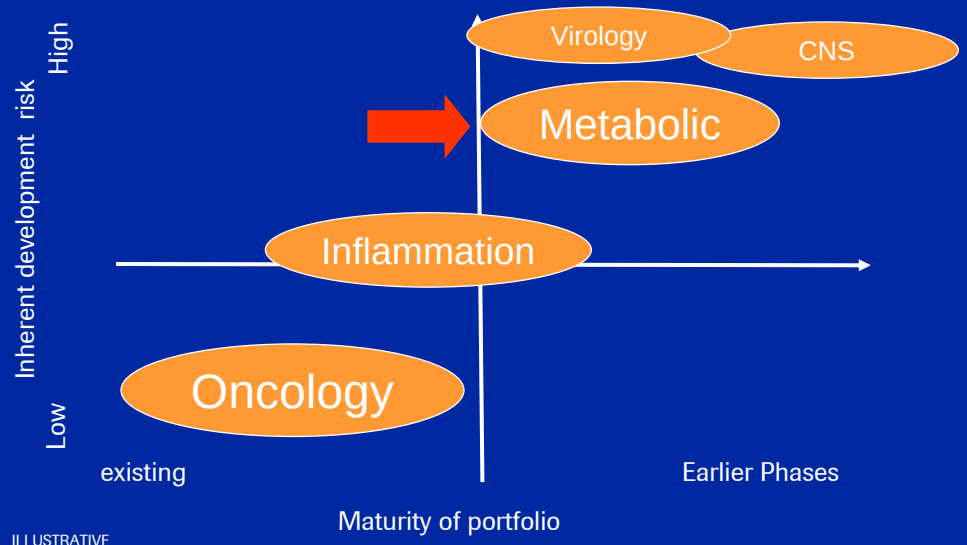
Large international phase III program

- 5 registration trials (>4'000 patients)
- Mono and combo therapy
- Patient populations studied:
  - MTX inadequate responders
  - DMARD inadequate responders
  - Anti-TNFα inadequate responders
  - MTX naïve patients
- **First 4 trials all met primary endpoint**

Global filing Nov 2007

Key drivers for long term development in place

Develop the short term drivers while not 'leaving ' the others



ILLUSTRATIVE

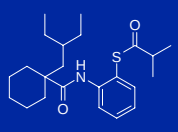
Metabolic Portfolio
Promising Late-Stage Assets

- CETPi first phase III entry
- Compounds approaching phase III
  - GLP-1
  - DPP-IV
  - Aleglitazar
- Update on Diabetes portfolio at ADA, June 2008

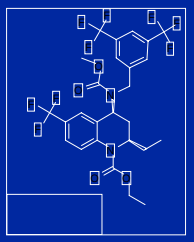
CETP Inhibitors
R1658 is a unique CETPi

- In contrast to the majority of other CETPi, R1658 has a different chemical backbone to Torcetrapib
- In patients treated with R1658, HDL is of normal composition
- In pre-clinical models and in clinical trials up to phase II, data showed that R1658 at therapeutic doses had a similar safety profile to placebo, including effects on blood pressure and RAAS activation

R1658

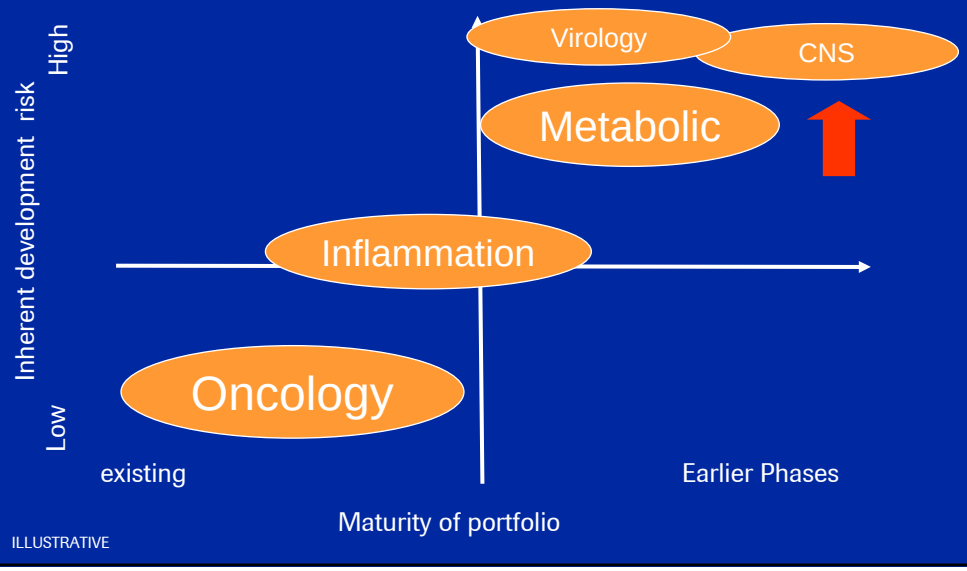


Torcetrapib



Key drivers for long term development in place

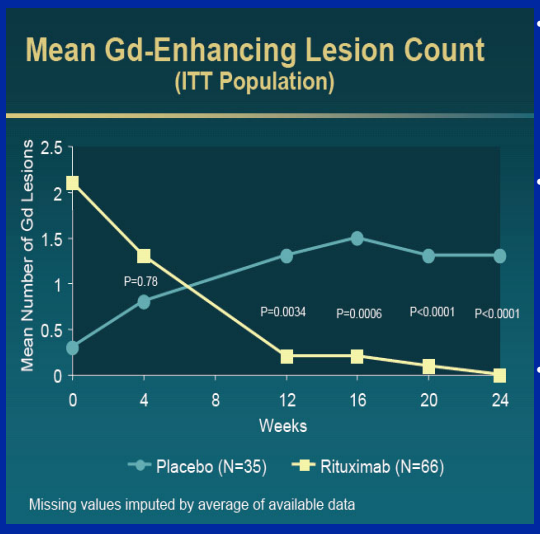
Develop the short term drivers while not 'leaving ' the others



ILLUSTRATIVE

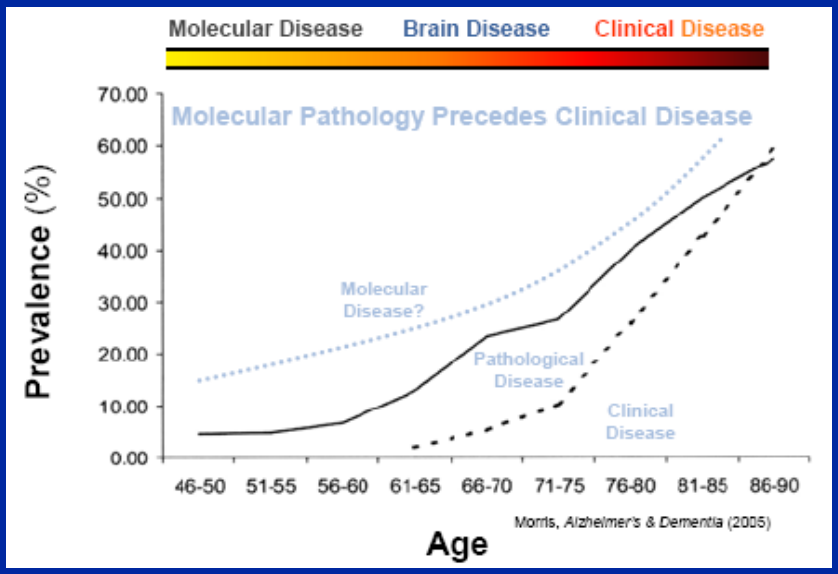
New market opportunities: Anti-CD 20 Strategies in MS

Very promising signals from Phase II



- Total cumulative mean number of gadolinium lesions was reduced by 91 %, p<0.0001)
- Patients with relapses over 24 weeks in the treated arm was 14.5 % compared to 34.3 % in the placebo (58 percent relative reduction, p = 0.0238)
- Ocrelizumab Phase II placebo-controlled program ongoing in RRMS

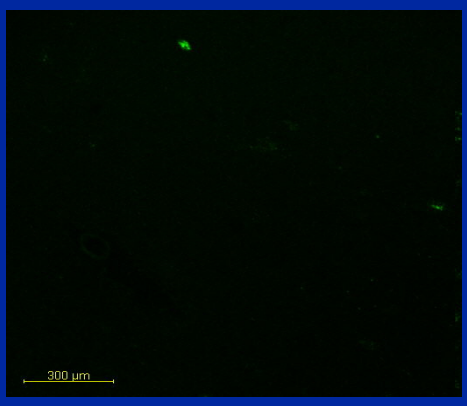
Future Role of Biomarkers – Prodromal AD



Efficacy of RO4909832 (mAb-31) *In Vitro*

Removal of plaques from human AD brain

- Postmortem sections of human AD brain incubated with mAb-31 and human monocytes
- Increased concentrations cause increased clearance of amyloid plaques



Control

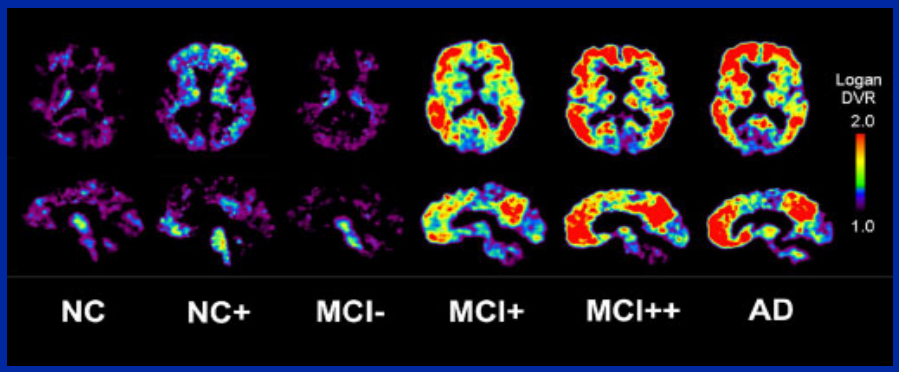
Dose 1

Dose 2

Dose 3

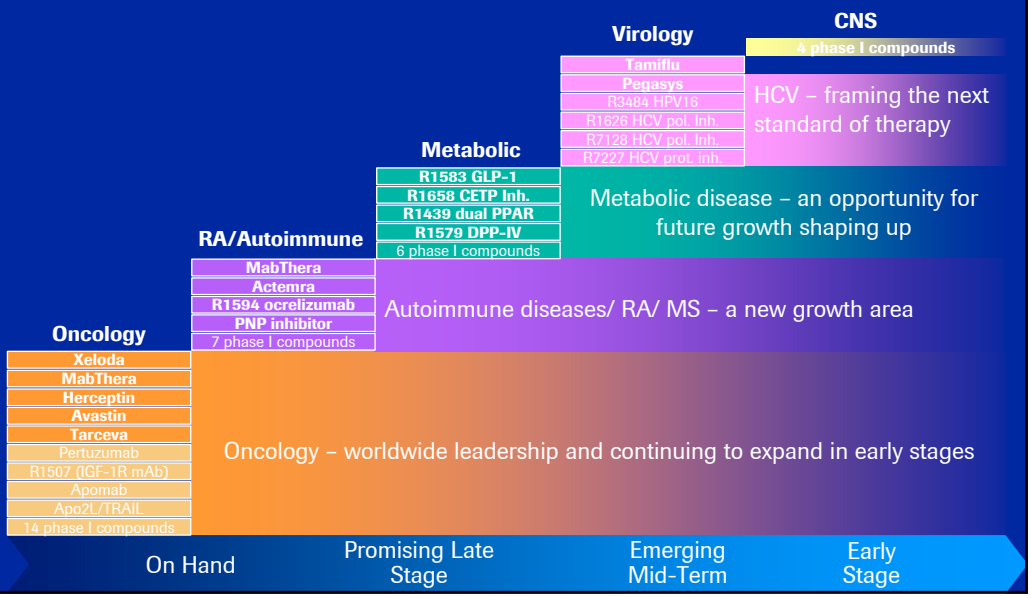
Dose 4

11C-PIB to measure amyloid load



Mathis et al.
Nucl Med Biol 2007; 34(7); 809-22

Roche key therapeutic areas
Current and future pillars of growth




Roche
We Innovate Healthcare