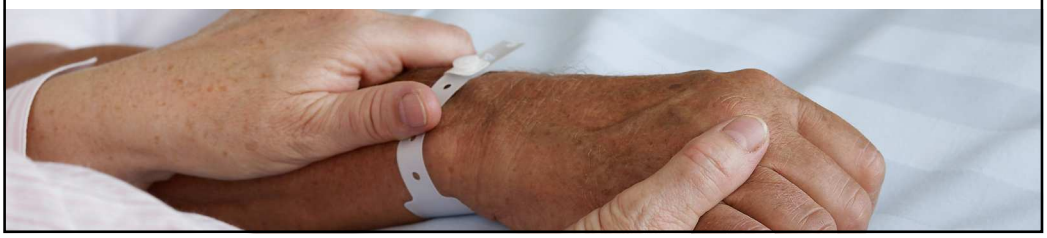
Clinical Development at Roche: Driving the paradigm shift

Jean-Jacques Garaud, MD
Global Head Pharma Development, Chief Medical Officer Roche

Sell sider breakfast Paris, October 23, 2008



Personalized healthcare: Fashion or substance?

- Where the value goes
- Where we stand at Roche
- Pipeline update

Key Drivers of Change in Our Industry

Healthcare Pressures: Benefit-Risk Ratio

Economic Pressures: Benefit-Cost Ratio

New Technologies: Expanded Capabilities

Key Drivers of Change in Our Industry

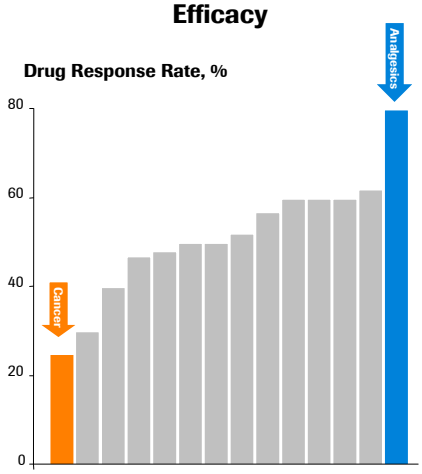
Healthcare pressures intensify focus on improved benefit-risk ratio

Patients are different, diseases are heterogeneous

However, most medicines are not differentiated

Key Drivers of Change in Our Industry
A call for more effective and safer drugs

Efficacy



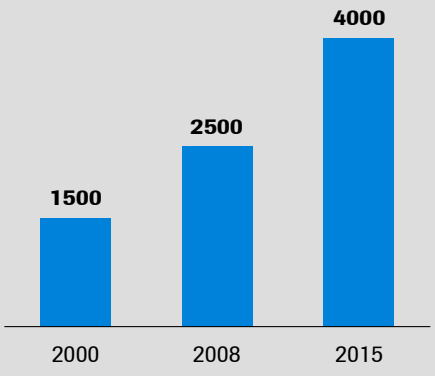
Safety

Avandia rosiglitazone maleate	GSK
ACOMPLIA rimonabant	Sanofi aventis
Mycograb®	Novartis
TRASYLOL (aprotinin injection)	Bayer
Zelnorm (tegaserod maleate)	Novartis

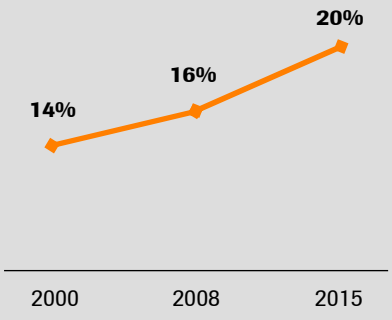
1 Spears et al., Trends Mol Med, 2001; 2 Lazarou et al., JAMA, 1998

Key Drivers of Change in Our Industry
Economic pressures intensify focus on improved benefit-cost ratio

U.S. Healthcare Spending, US$ Billions



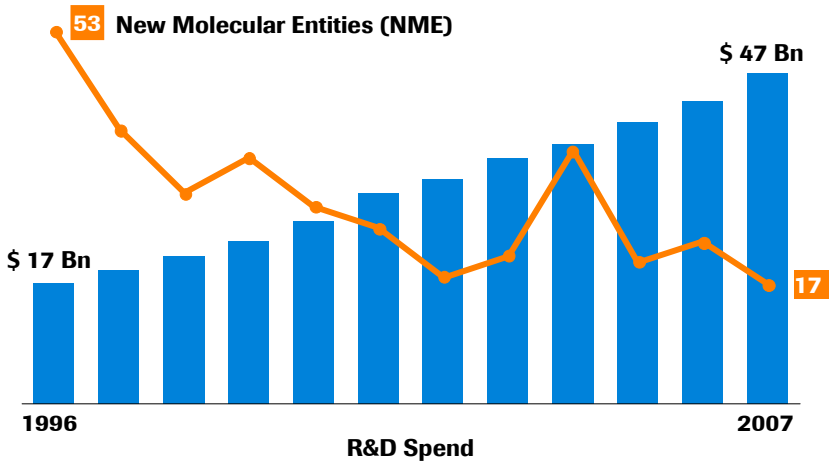
U.S. Healthcare Spend as % of GDP



Source: Centers for Medicare and Medicaid, Office of the Actuary, National Health Statistics Group

Key Drivers of Change in Our Industry

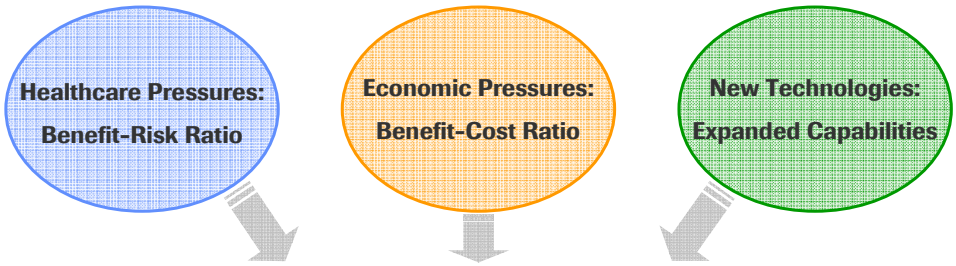
Step-change needed in Pharma development



Sources: FDA/CDER Data, PhRMA data, Price Waterhouse Coopers analysis, Pharma 2020

Key Drivers of Change Towards PHC

PHC is key to enabling highly differentiated medicines



Need for highly differentiated medicines that impact positively public health

Payors will reward innovation

Personalized Healthcare: Fashion or substance?

Where the value goes

Where we stand at Roche

Pipeline update

Defining Value

For patients and payors, better clinical outcomes and improved quality of life

Benefit to Patients & Payors can be:

- Better and more predictable clinical outcomes
- Quality of life and life-years gained
- Reduced morbidity
- Reduced unnecessary treatment/side effects and associated costs
- Better compliance

Defining Value

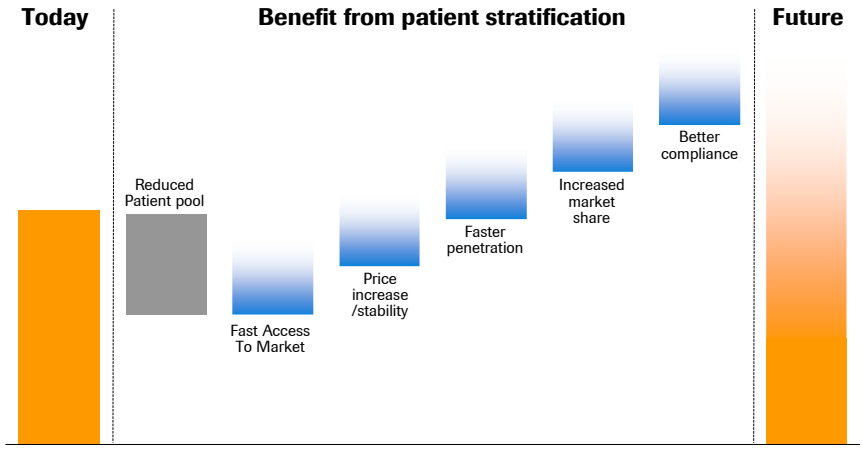
For Roche Pharma, faster market access and penetration

Benefit to Roche Pharma can be:

- Faster access to market
- Better and more stable pricing
- Faster penetration into market
- Increased market share
- Better compliance
- Longer duration of therapy

Pharmacoeconomics of Therapeutic Stratification

Reduced patient populations offset by increased total revenue and patient benefit



Defining Value

For Roche Diagnostics, high medical value tests yield higher growth and increased market share

Benefit to Roche Dx can be:

- New business with strategic growth
- Higher medical value tests, leading to premium pricing
- Higher placements of platforms
- Increased market share

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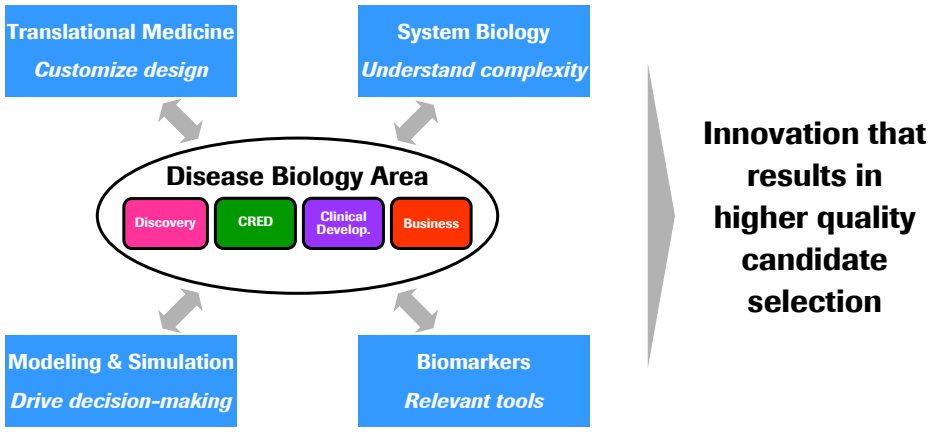
PHC in Roche – The Roche Group

Two highly complementary divisions that represent a natural fit

Built on a foundation of expertise in molecular biology and technologies

Pharma 2015 – New R&D Model

Bringing the right disciplines together at the center-stage of drug discovery & development



Collaboration Pharma and Diagnostics

Biomarker programs for all pharma projects

Example Oncology

Phase I and II		Phase III / market	
IGF-1R mAb (R1507)	• Range of candidate markers	Herceptin	• HER2 expression • HER2 gene amplification
MDM2 antag (R7112)	• P53 wild-type	Avastin	• Range of candidate markers for hypothesis investigation
PLX4032 (R7204)	• BRAF V600E gene mutation	Pertuzumab	• Range of candidate markers
T-DM1 (R3502)	• HER2 expression • HER2 gene amplification	Tarceva	• EGFR expression (IHC) • EGFR gene copy number (FISH) • EGFR mutations • KRAS mutations

Summary …

… in a few words

1. It is Real!
2. Optimal value: Start early, own IP and co-launch
3. Our unique position: Pharma and Dx, new R&D model

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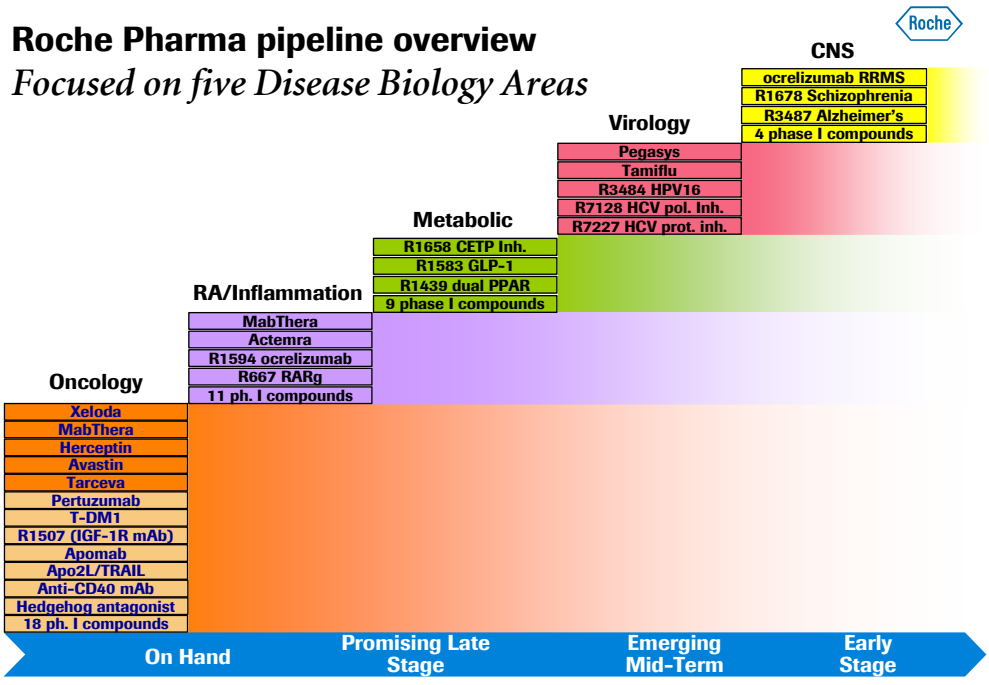
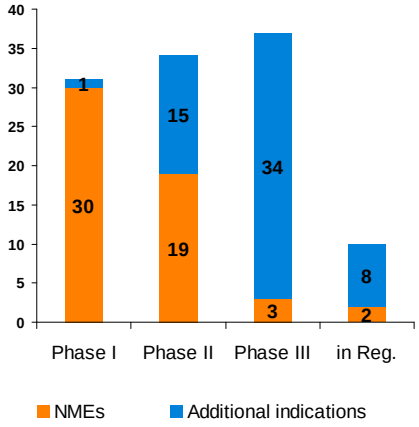
Roche Pharma pipeline overview

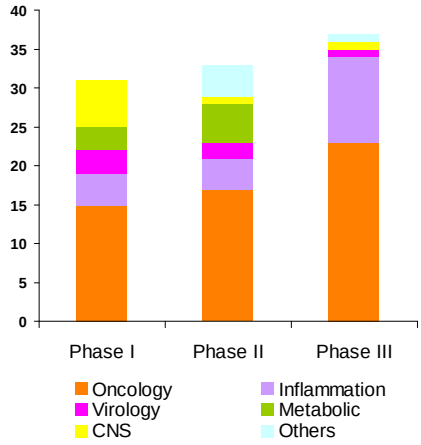
Focused on five Disease Biology Areas



Pipeline: 54 NMEs and 58 additional indications

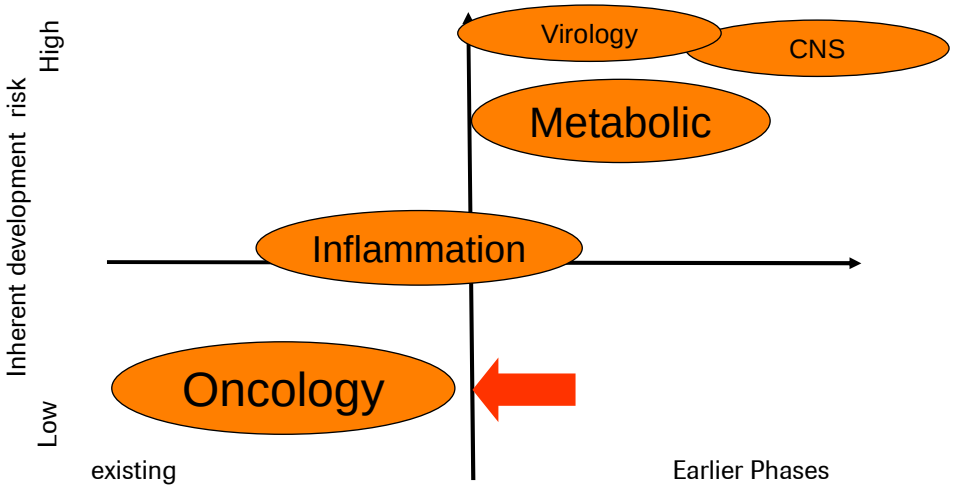
Staying strong in oncology and diversifying into new areas





Key drivers for long term development in place

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



ILLUSTRATIVE

Oncology: Q3 '08 pipeline update

Significant newsflow before end of year

MabThera in relapsed CLL: REACH ✓

Randomized ph. III, 552 patients
Fludarabine+cyclophosphamide
+/-MabThera
met primary endpoint (PFS)

Filing 2009

Tarceva+Avastin in 2nd line NSCLC: BETA lung ✓

Tarceva+/-Avastin
improvement in PFS / RR benefit
OS not significant

EU filing under evaluation

Avastin in 1st line mBC: RIBBON-1

Phase III study, 1238 patients,
2 primary analyses:
Anthracycline-/taxane-based +/- Avastin,
and Xeloda +/- Avastin

Expect topline data Q4 '08

Tarceva 1st line maintenance NSCLC: SATURN

4 chemo cycles followed by T vs. placebo
Enrollment completed Q2 '08
Potentially label-enabling for Tarceva

Expect topline data Q4 '08

Avastin still early in its journey

Realising full potential across tumour types

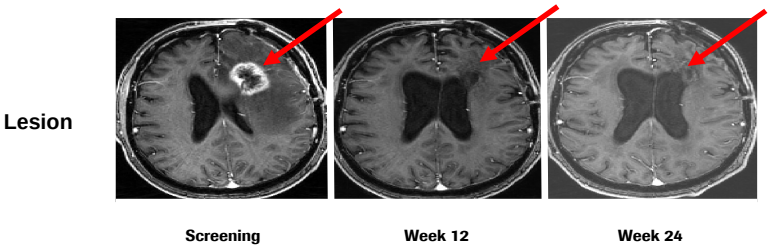
Tumour	Early/adjuvant (Potential for cure)	Advanced/metastatic (Extending life) 1st-line of treatment	Advanced/metastatic (Extending life) 2nd-line of treatment
Colon, colorectal	**Phase III** (AVANT, NSABP C-08)	✓ **Launched** [EU, US, JP; broad label in 1st and subsequent lines]	
Lung (NSCLC)	**Phase III** (E1505)	✓ **Launched** [EU majority of chemos, US carboplatin/paclitaxel]	**Phase III** (BETA Lung w/Tarceva)
Breast (HER2-)	**Phase III** (BEATRICE, E5103)	✓ **Launched** [EU, US w/paclitaxel] **Phase III** (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 tested in gastric, ovarian and prostate cancer, aNHL, and brain (GBM)

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

Avastin in Refractory Glioblastoma Multiforme (GBM)

High unmet medical need



- Incident Primary Brain Tumors population in line with mRCC
  - 20,000 incident patients in top 5 EU countries (mRCC: 17,000)
- Phase II data demonstrated encouraging six-month PFS and ORR in patients with relapsed GBM, exceeding historical estimates of 15%
- Avastin in relapsed GBM ph. II data on track to be filed by end 2008
- Phase III in first-line Glioblastoma in preparation

25

T. F. Cloughesy et al., ASCO 2008, abstract 2010b (Monday)

Maintaining leadership in oncology

Building on our key areas of expertise

New molecular entities	Key features	Potential patient benefit	Stage of development
Anti-CD 20 (building on MabThera)			
R7159/GA101 (3rd generation)	Glyco-engineered type II antibody, fully humanized; ADCC↑, CDC↓ direct cell death↑	Significantly improved efficacy	ph. I /II NHL, CLL
Anti-HER2 (building on Herceptin)			
Pertuzumab	Inhibition of HER2 dimerisation	Improved efficacy in combo with Herceptin	ph. III mBC ph. II mNSCLC
Trastuzumab-DM1	Anti-microtubule linked to Herceptin	Reduced side effects, superior efficacy	ph. II mBC ph. III 'go'
Angiogenesis (building on Avastin)			
R7334 / TB-403 Anti-PlGF mAb	mAb against placental growth factor (PlGF); blocks a pro-angiogenic factor	Adding efficacy to Avastin in combo or sequentially	ph. I

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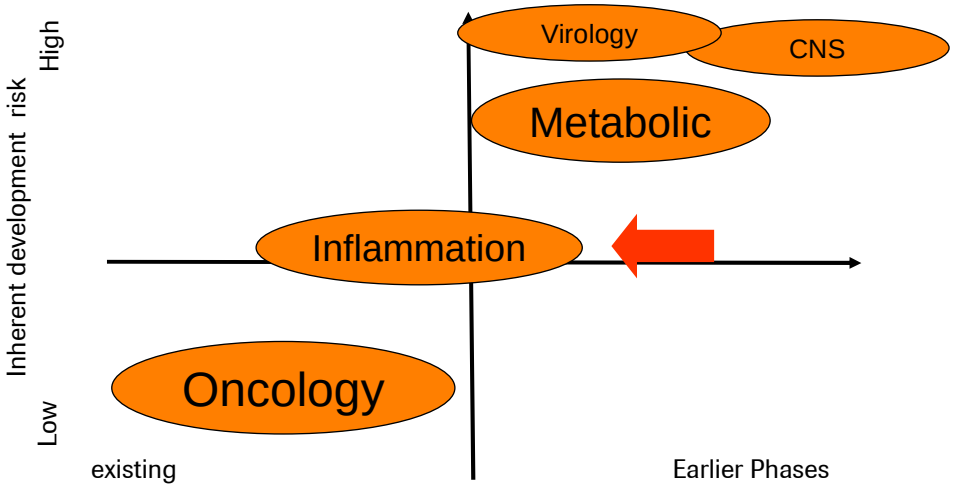

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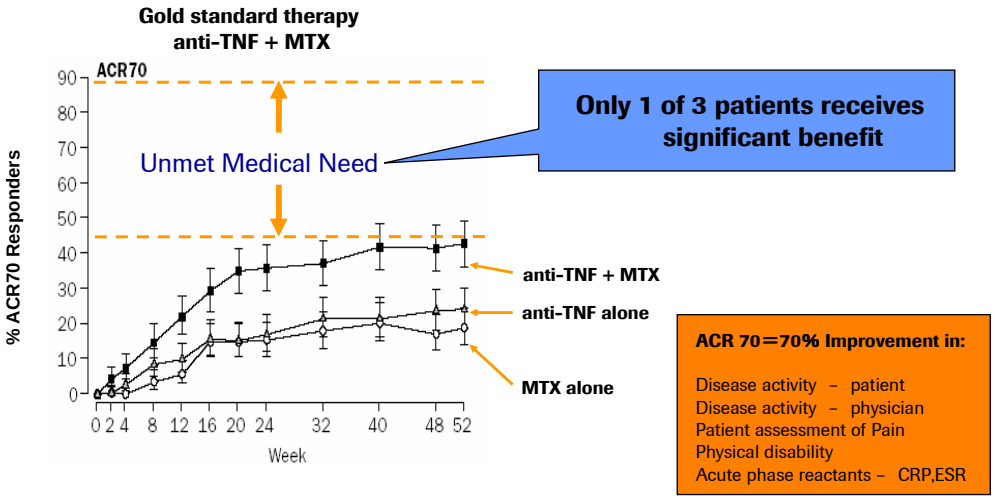
Rheumatoid Arthritis: Not all patients respond to current therapy

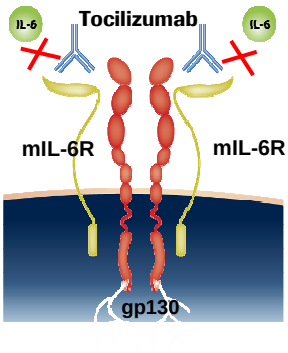


ACR 70=70% Improvement in:

Disease activity – patient
Disease activity – physician
Patient assessment of Pain
Physical disability
Acute phase reactants – CRP,ESR

Actemra: The first IL-6 receptor inhibitor

Unprecedented level of remission in moderate to severe patients with RA



- Largest clinical programme of any biologic for RA
- Consistently high & durable remission rates - across different disease stages
- Rapid treatment response - as early as 2 weeks

New data presented at EULAR 2008:

- RADIATE: Rapid and significant improvements in patients who have failed up to 3 anti-TNF inhibitors[1]
- AMBITION: Only biologic to have demonstrated superiority vs. methotrexate as monotherapy[2]
- Regulatory update: Positive FDA panel on July 29th 2008; CRL[3] received; working with FDA to address outstanding matters, EU review on track

1 Emery et al., EULAR 2008, Abstract OP-0251 2 Jones et al., EULAR 2008, Abstract OP-0131 3 Complete response letter

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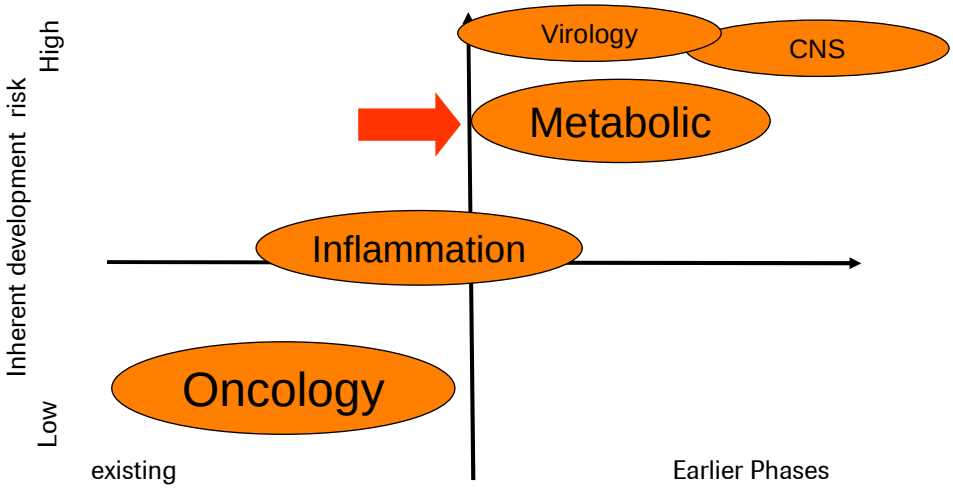
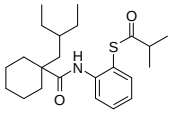


ILLUSTRATIVE

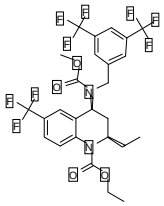
CETP Inhibitor
R1658 is a unique CETPi

- 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

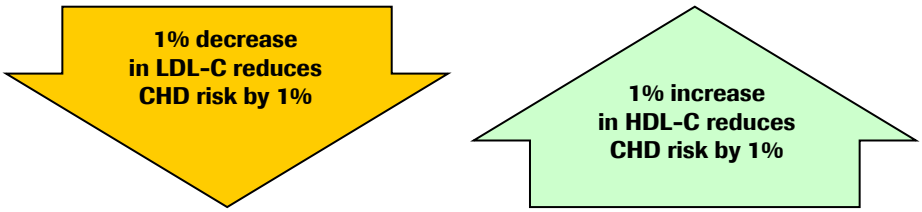
R1658 (Dalcetrapib)



Torcetrapib



Relationship Between Changes in LDL-C and HDL-C Levels and CHD Risk



Third Report of the NCEP Expert Panel. NIH Publication No. 01-3670 2001.

Large mortality and morbidity study running

- Only true evaluation of the CV benefits of raising HDL-C by CETPi
- R1658 is being investigated to reduce CV risk on top of current recommended standard of care for CV risk factors
- Currently the only route to approval of CETPi

Taspoglutide: investigational once-weekly GLP-1 analogue for the treatment of type-II diabetes

- Significantly reduces blood glucose over only eight weeks
- Provides substantial weight loss in a dose-response fashion
- Additional titration study confirmed the safety and tolerability of taspoglutide
- Efficacy, safety and tolerability profile encouraging
- Phase III recruitment started in Q3 2008

Taspoglutide (R1583) has the potential to be the first once weekly, long-acting human GLP-1 analogue

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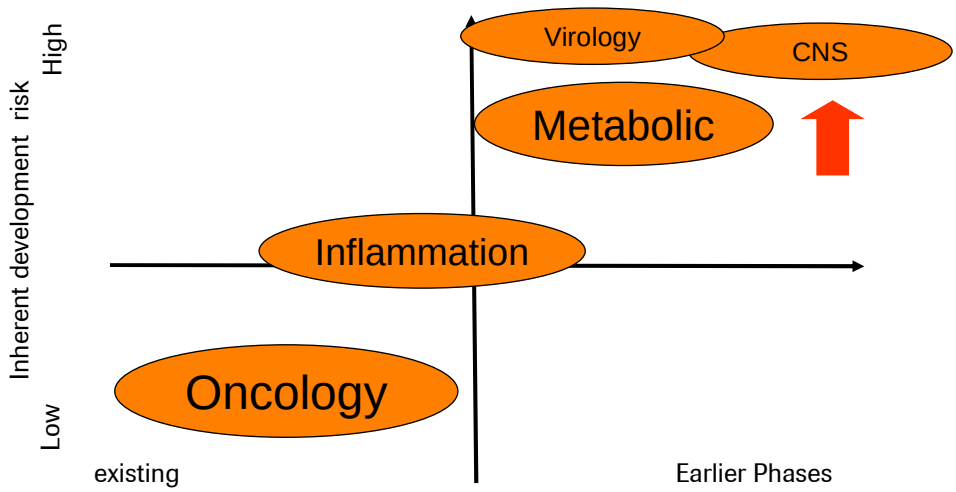
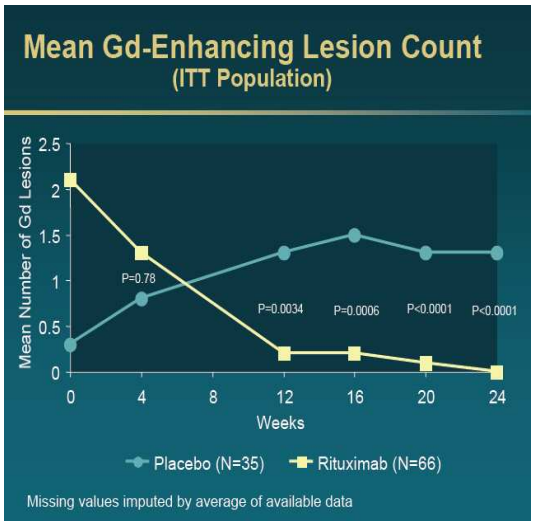


ILLUSTRATIVE

CD20 targeting: new treatment strategy for MS

Very promising signals from Phase II with rituximab



- 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 in RRMS

Roche R&D opportunities in summary

- Innovation-driven business focused on differentiated products that add medical value
- Network approach to foster innovation and build on our core business
- Leverage combination of Pharmaceuticals and Diagnostics in-house to develop more targeted treatment options (personalized healthcare)
- Numerous short- and mid-term drivers of growth with low development risk
- Broad pipeline for long-term sustainable growth

Our unique strategy provides Roche with a competitive edge for sustainable outperformance

We Innovate Healthcare