

## Roche

### Positioning AVASTIN-based therapy as essential to treat cancer

*Dr. Karl Mahler, Head of Investor Relations*  
*Dr. Stefan Frings, Life Cycle Leader Avastin*



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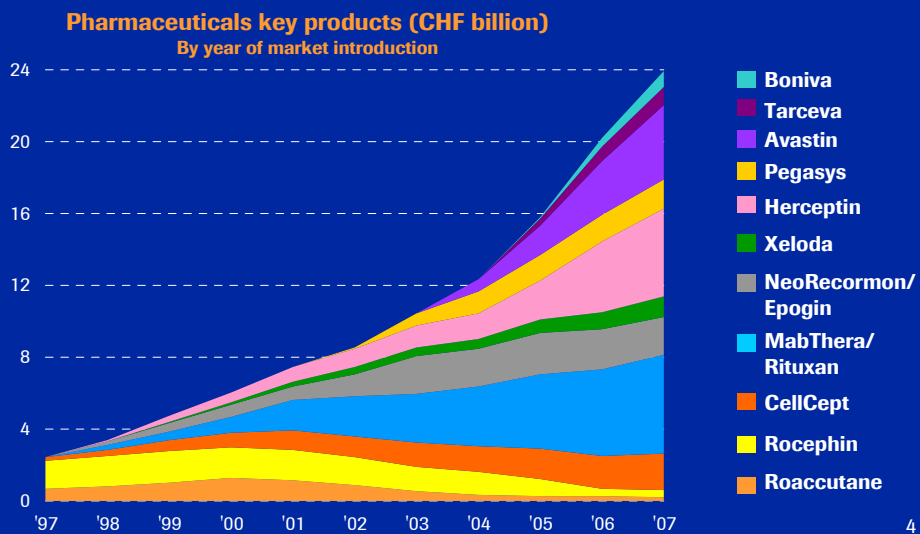
## Introduction

## Update on Avastin

## Summary

## Differentiated and rejuvenated product portfolio

*From 1 to 9 products with sales around or above CHF 1 billion*



**Our oncology strategy: Move the standards of care**



*New tumor types, new combinations, new lines of intervention*

**Clinically differentiated product**

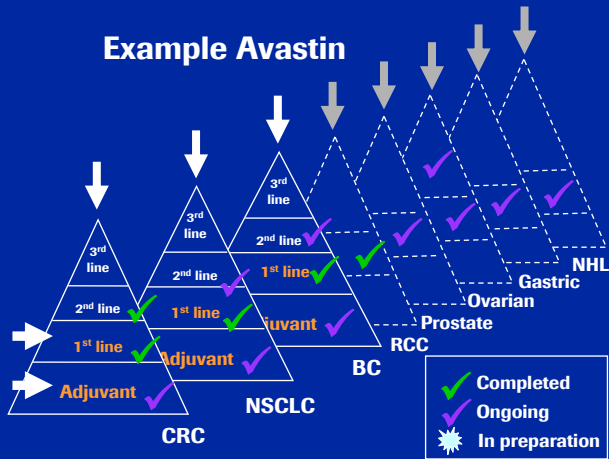
target all tumor types

target all important combinations

target earlier (adjuvant) intervention

**Superior outcome for patients**

**Example Avastin**



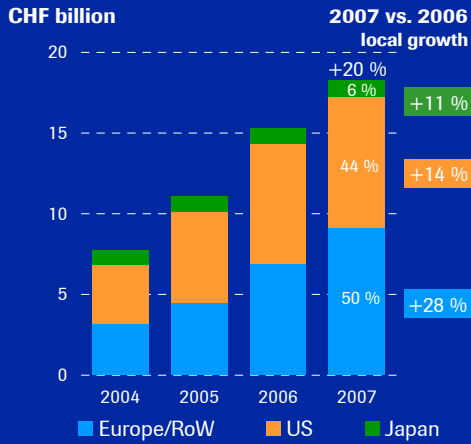
**Introduction**

**Update on Avastin**

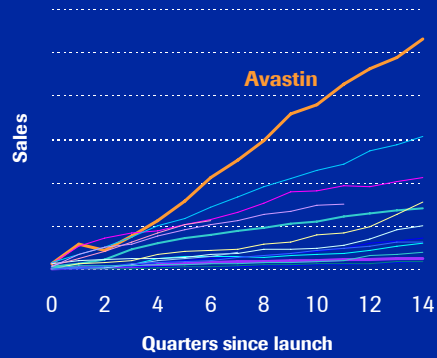
**Summary**



# Roche Oncology: Strongest growing franchise Avastin: Best growing oncology brand ever



Avastin launch compared to other cancer therapies (US plus top-5 EU markets<sup>1</sup>)

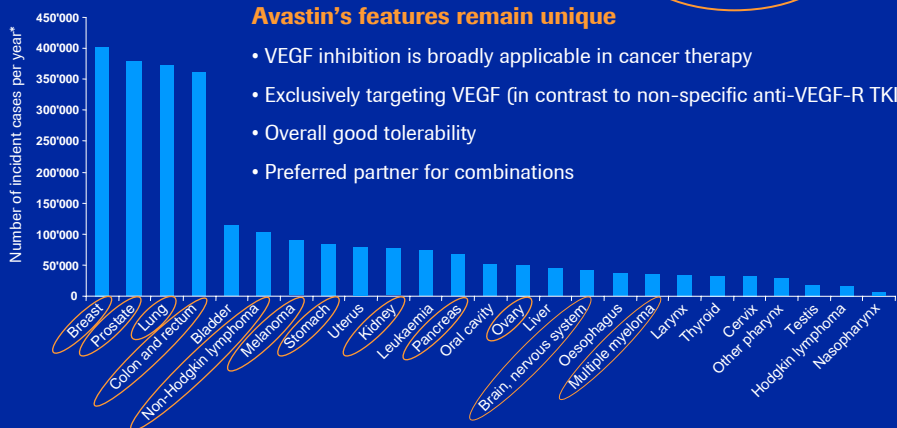


<sup>1</sup>Source: IMS. Products included are Avastin, Alimta, Arimidex, Camptosar, Eloxatine, Erbitux, Femara, Gemzar, Herceptin, MabThera, Nexavar, Sutent, Tarceva, Taxol, Taxotere, Xeloda

## Avastin Backbone of cancer therapy



Major cancers tested with Avastin



\*in USA plus top 5 EU countries

## Avastin still early in its journey

### Realising full potential across tumour types



Tumour	Early/adjvant (Potential for cure)	Advanced/metastatic (Extending life)	
		1 <sup>st</sup> -line of treatment	2 <sup>nd</sup> -line of treatment
Colon/ rectal	Phase III (AVANT, NSABP C-08, E5202, E5204)	✓ <b>Launched</b> [EU, US, JP; broad label in 1st and subsequent lines]	
Lung (NSCLC)	Phase III (E1505)	✓ <b>Launched</b> [EU majority of chemos, US carboplatin/paclitaxel]	Phase III (BETA Lung w/Tarceva)
Breast (HER2-)	Phase III (BEATRICE, E5103)	✓ <b>Launched</b> [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)	-	✓ <b>Launched</b> [EU; with interferon]	

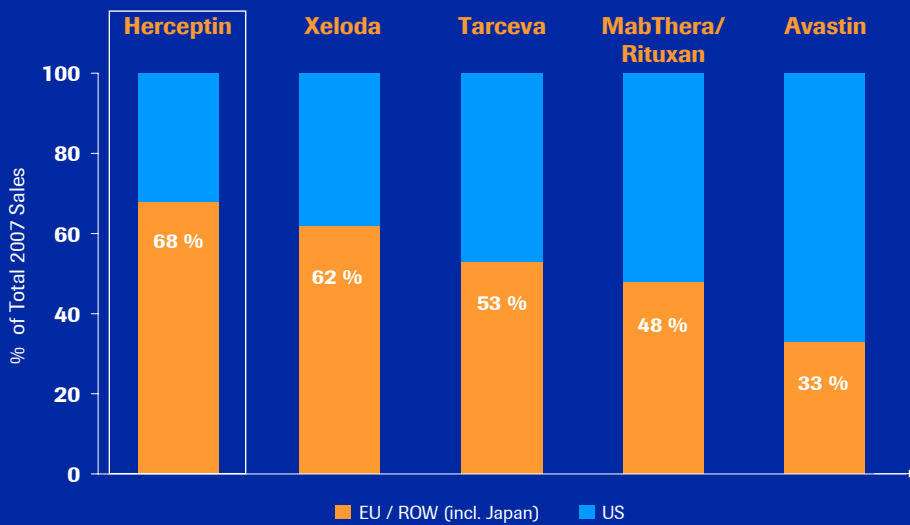
**Avastin also trialed in gastric, ovarian, prostate, aNHL, and brain (GBM)**

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

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## Major growth opportunities outside the US

### Herceptin leading the way

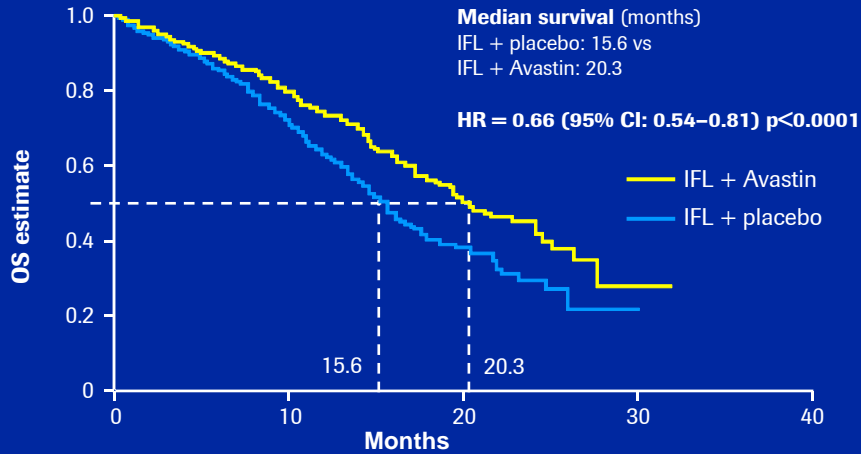


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## Avastin in 1<sup>st</sup> line mCRC



*Largest improvement in overall survival in phase III*



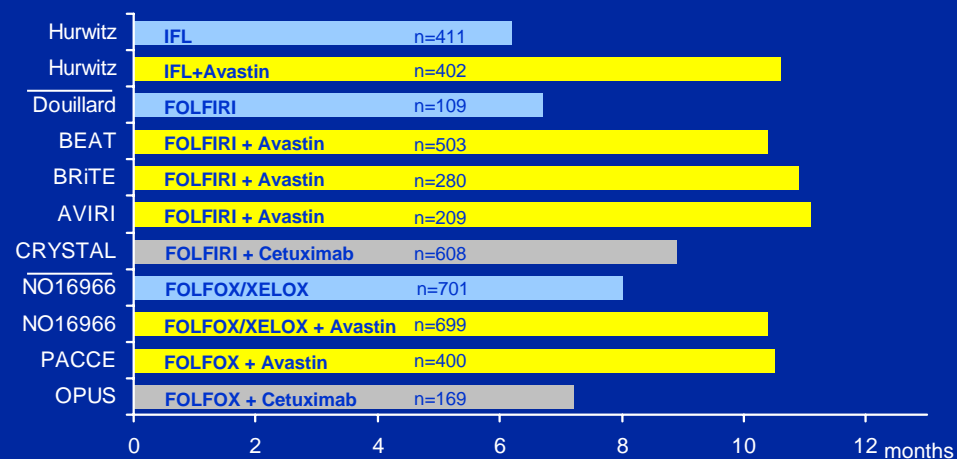
CI = confidence interval; IFL irinotecan, bolus 5-FU/FA  
 H. Hurwitz, et al. *NEJM* 2004;350:2335-42

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## Avastin in 1<sup>st</sup>-line mCRC



*Consistently delivers the best PFS outcome*

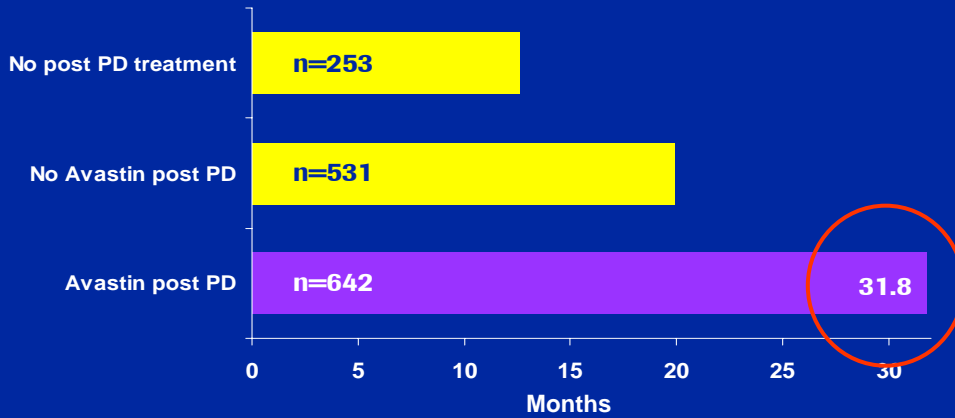


**Avastin: The only biologic agent with OS benefit in 1<sup>st</sup>-line mCRC**  
**Adds benefit to all chemotherapies**

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## BRiTE: post 1st progression therapy

*Avastin beyond progression: potential to increase survival*



**Superior survival in patients continuing Avastin beyond progression demonstrated in a multivariate analysis (HR=0.53, p < 0.001)**

A. Grothey et al. ASCO 2007

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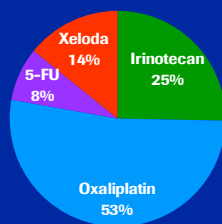
## Expanding the market for Avastin and Xeloda in mCRC

*Avastin to be combined with any chemo in any line of treatment*



### Avastin

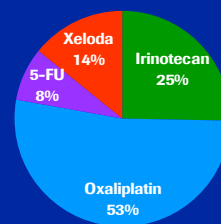
Current EU label:  
5-FU or 5-FU + Irinotecan



New EU label:  
Any fluoropyrimidine combination



### Xeloda



New EU label:  
Any combo, including with Avastin



Source: Synovate Healthcare 2005

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## Avastin in mCRC

### Conclusions

#### Four randomized trials show compelling efficacy

- AVF2107g
- E3200
- AVF2192
- NO16966

#### Aiming for cure

- High rates of surgeries with curative intent shown in BEAT and NO16966
- Resection rates for 'liver mets only' patients in NO16966: 19.2% in Avastin arm (vs 12.9%)
- Secondary resection as a concept is promising, but requires further investigation

**Incidence: 155,000 cases<sup>1,2)</sup>**

<sup>1)</sup> US and top 5 EU, <sup>2)</sup> stage IV

## Avastin in adjuvant colon cancer

### Key phase III trials fully recruited

#### NSABP C-08

#### AVANT

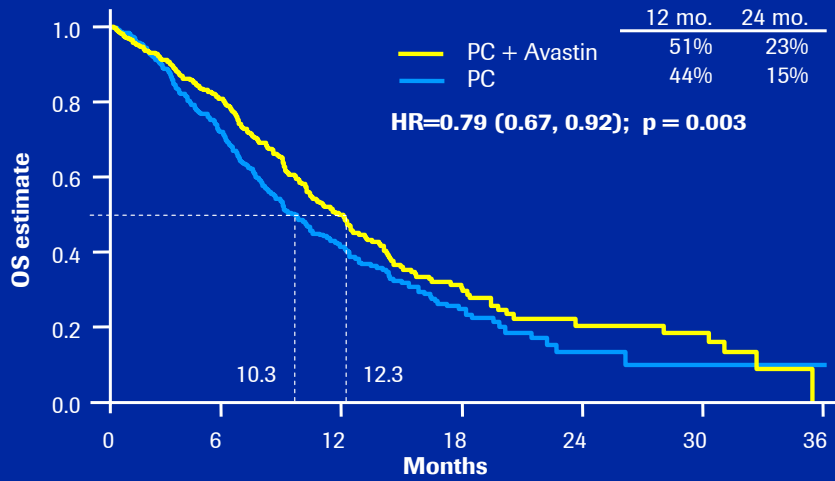
	NSABP C-08	AVANT
<b>Treatment regimen</b>	FOLFOX-6 ± Avastin	FOLFOX-4 ± Avastin XELOX + Avastin
<b>Number of patients</b>	2,700	3,450
<b>Recruitment duration</b>	Q3 2004 until Q4 2006	Q4 2004 until Q2 2007
<b>Efficacy analysis</b>	First interim look: Q2 2007 Subsequently every 6 months Next interim look: Q2 2008	Event-driven analysis
<b>Filing</b>	2010 (or earlier)	2010 (or earlier)

**Incidence: 150,000 cases<sup>1,2)</sup>**

<sup>1)</sup> US and top 5 EU; <sup>2)</sup> stage II high risk, and stage III

## Avastin in 1<sup>st</sup> line NSCLC (E4599)

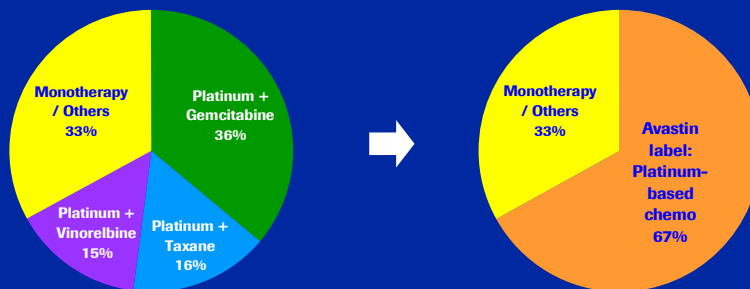
First drug in a decade to show an overall survival benefit



A. Sandler, et al. NEJM 2006 PC= paclitaxel/carboplatin

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## Avastin launching with best-possible label in 1<sup>st</sup>-line NSCLC market in Europe<sup>1</sup>



Avastin in combo with all current standards (platinum)

Source: Synovate Healthcare, MAT Q3 2007; <sup>1</sup> in non-squamous NSCLC

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## Avastin in 1st line NSCLC

### *Conclusions*

- First front-line treatment to demonstrate extended survival in over a decade
- Efficacy demonstrated in two randomized phase III trials (E4599 and AVAiL)
- Generally well tolerated
- Approved in US and approved in EU with a broad label
  - in combination with any platinum-based chemotherapy regimens
  - at least 50% of NSCLC population covered

**Incidence: 275,000 cases <sup>1, 2)</sup>**

<sup>1)</sup> US and top 5 EU, <sup>2)</sup> stage IIIb and IV

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## Avastin in adjuvant lung cancer

### *High unmet medical need*

- Phase III E1505
  - Stage IB to IIIA adjuvant squamous and non-squamous NSCLC
  - 1500 patients
  - Started Q3 2007
  - Chemotherapy +/- Avastin (15 mg/kg q3 weeks)
  - Limited therapeutic options currently available

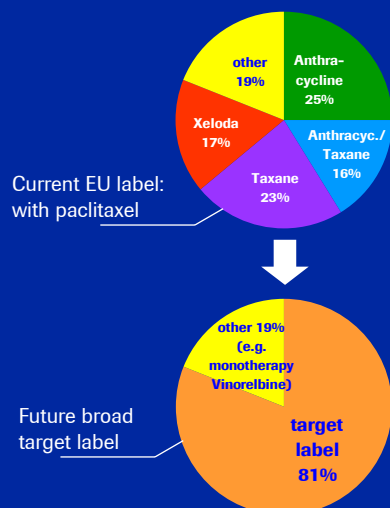
**Incidence: 135,000 cases <sup>1)</sup>**

<sup>1)</sup> US and top 5 EU

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## Establishing Avastin in metastatic breast cancer

*Strong commitment*



### US submission for 1<sup>st</sup> line mBC

- ODAC split vote Dec 5, 2007
- FDA action date Feb 23, 2008

### Further phase III studies im mBC to report in 2008

- AVADO (docetaxel +/- Avastin): primary objective met Feb 2008
- RIBBON-1 (var. chemos +/- Avastin): data expected in H2 2008

**Incidence: 100,000 cases <sup>1,2)</sup>**

Source: Genactis MBC study Q4 2005

<sup>1)</sup> US and top 5 EU, <sup>2)</sup> stage IV, HER2-pos. and neg.

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## Avastin in adjuvant breast cancer

*Large opportunity – major phase III trials started*

	Phase II E2104	Phase III E 5103	Phase III BEATRICE	Phase III BETH
Patient population	HER2-negative	HER2-negative	HER2-, ER-, PR-negative	HER2-positive
Number of patients	226	4950	2530	~3600
Design	Anthracyclines + Avastin followed by paclitaxel + Avastin ( 2 arms)	AC +/- Avastin followed by paclitaxel +/- Avastin (3 arms)	Antracycline or taxane-based chemos +/- Avastin	Chemo + Herceptin +/- Avastin
Primary endpoint	safety	Disease-free survival	Disease-free survival	Disease-free survival
Status	Initial safety results presented at SABCS 2007	FPI Q4 2007	FPI Q4 2007	Expect FPI H1 2008

**Incidence: 320,000 cases <sup>1)</sup>**

<sup>1)</sup> US and top 5 EU

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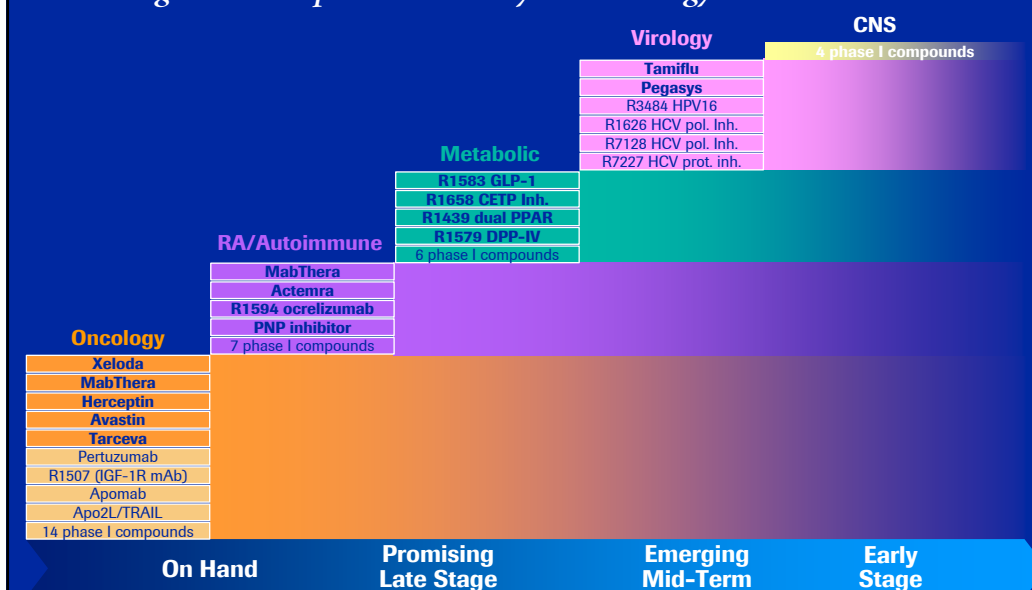
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## Roche key therapeutic areas

*Entering new therapeutic areas beyond oncology*



## Roche: A unique investment case



- **Clear and focused strategy**
  - Medically-differentiated products; poised to become leader in Personalized Healthcare
- **Attractive risk profile**
  - Low generic risk; lowest among European large-cap players
  - 42 phase III projects; many additional indications
- **Assets in place for sustained success**
  - World market leader in Oncology
  - Emerging Rheumatology & Autoimmune franchises
  - Promising phase II pipeline in Diabetes, Metabolism; early-stage compounds in CNS and Virology
- **Industry-leading organic growth & value creation**
  - 2007: Sales +10 %, Core EPS +20%

Unique high-tech healthcare investment

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## Our objectives for 2008



### Sales

- High single-digit local currency sales increase for Roche Group (excl. Tamiflu pandemic<sup>1</sup>)
- Above-market sales growth<sup>1</sup> in both divisions

### Core EPS

- Core earnings per share target<sup>2</sup> at least at record 2007 level despite significant increase in R&D investment and considerably lower Tamiflu pandemic sales

### Shareholder return

- Continuous increase in dividend pay-out ratio over the next 3 years

<sup>1</sup> Excluding government and corporate stockpiling orders of Tamiflu for pandemic use  
<sup>2</sup> At constant exchange rates

Barring unforeseen events

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