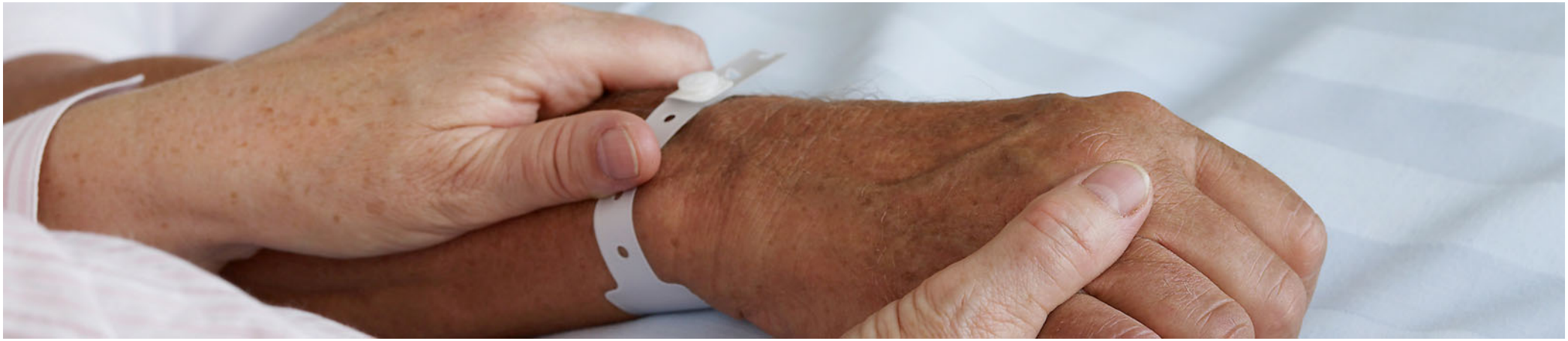
Clinical Development at Roche: Driving the paradigm shift

Jean-Jacques Garaud, MD
Head of Pharma Research & Early Development (pRED)

Cowen Group Healthcare Conference
March 8, 2010



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:

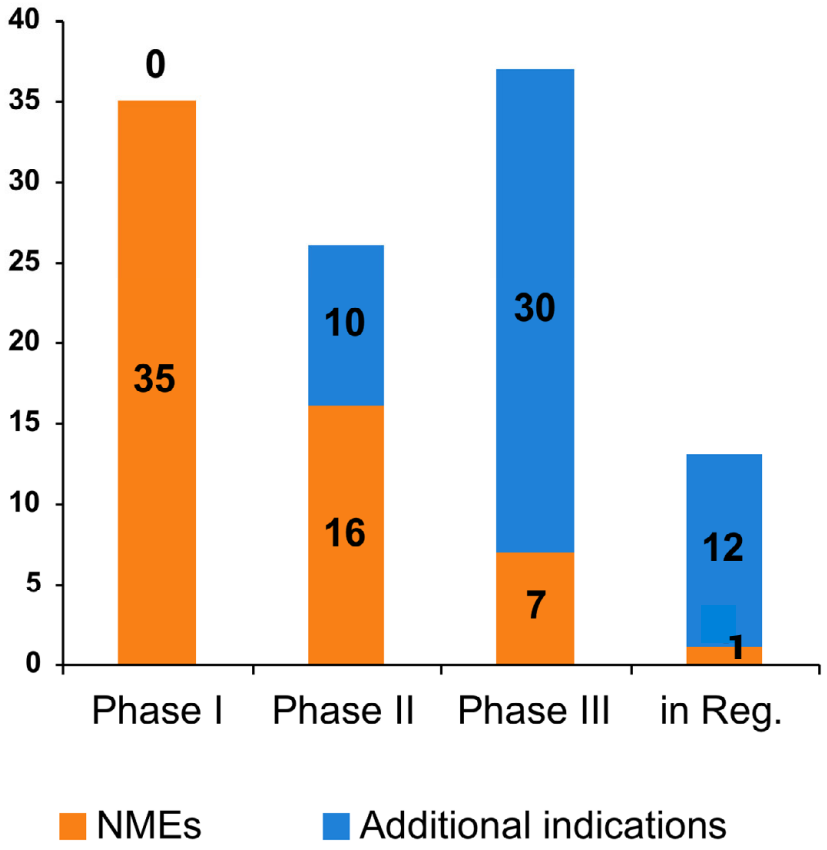
1 pricing and product initiatives of competitors;
2 legislative and regulatory developments and economic conditions;
3 delay or inability in obtaining regulatory approvals or bringing products to market;
4 fluctuations in currency exchange rates and general financial market conditions;
5 uncertainties 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.

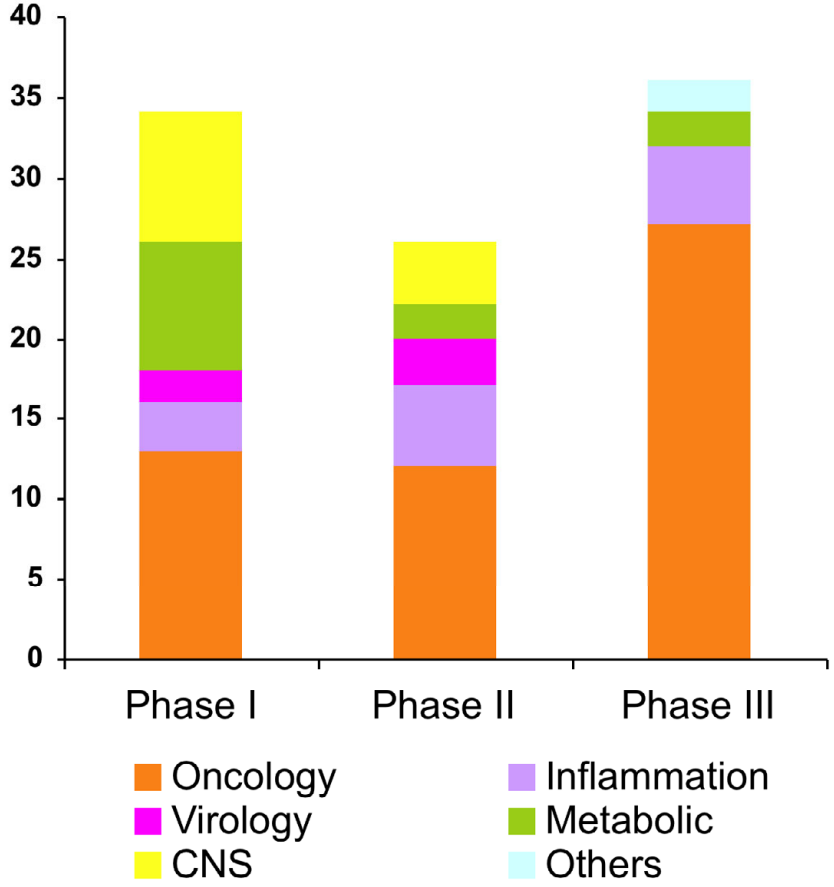
Any statements regarding earnings per share growth is not a profit forecast and should not be interpreted to mean that Roche’s earnings or earnings per share for this year or any subsequent period will necessarily match or exceed the historical published earnings or earnings per share of Roche.

For marketed products discussed in this presentation, please see full prescribing information on our website – www.roche.com

Roche Group Pipeline: 59 NMEs and 52 additional indications

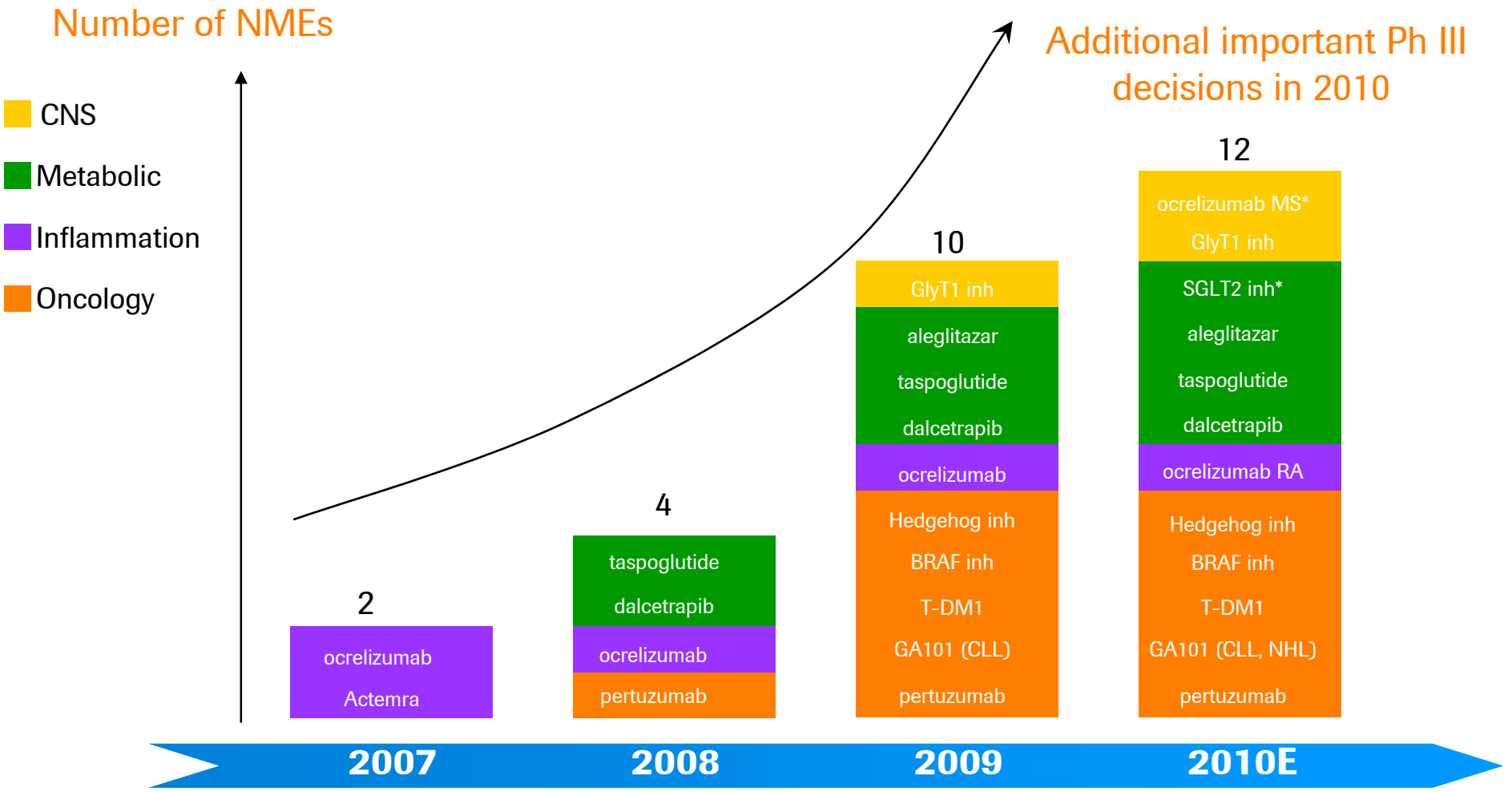
Staying strong in oncology and diversifying into new areas





Late-stage pipeline continues to build up

Expanding into new therapeutic areas

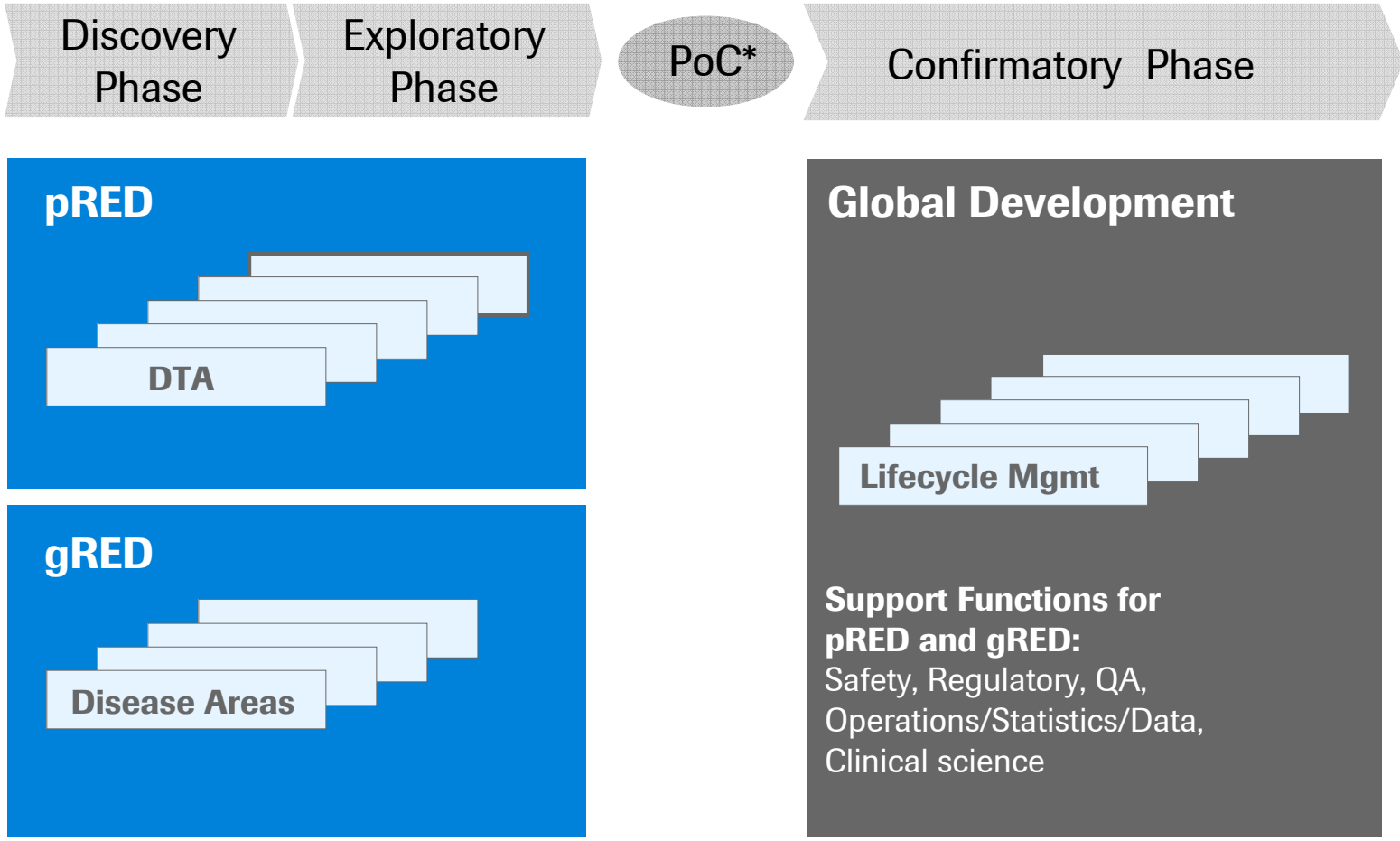


* Expect LIP decision in 2010

A rich and diverse pRED portfolio

Increasing depth across therapeutic modalities

Portfolio decisions focused on advancing important new therapies to address unmet medical needs



pRED: Pharma Research and Early Development
gRED: Genentech Research and Early Development

* Proof of Concept

The pRED mission

Science and patients: our focus, our passion

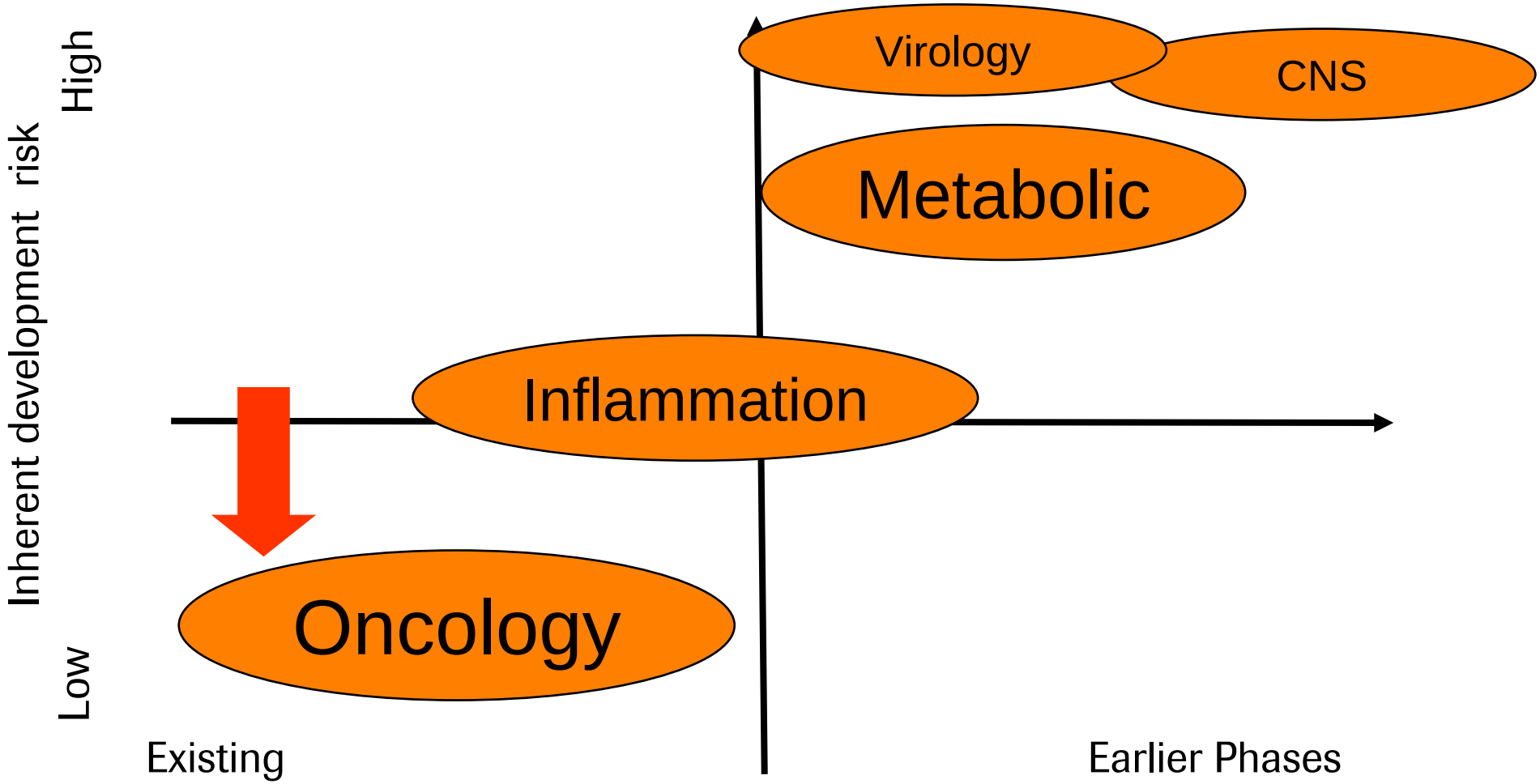
- Translate understanding of disease biology in the clinical setting
- Leverage technologies and capabilities to develop new compounds to the Lifecycle Investment Point (LIP)
- Deliver on individual patient needs through implementation of personalized healthcare strategies

Six transitions from pRED to late stage between 2007-2009:

• **Dalcetrapib**	• **GA101**
• **Aleglitizar**	• **B-RAF inhibitor**
• **Taspoglutide**	• **Glyt-1 inhibitor**

Key drivers for long term development in place

Develop the short-term drivers while not neglecting the long-term



ILLUSTRATIVE

Understanding Biology to Improve Patient Outcomes

Cancer Type	Marketed Products	Key Products in Development
Gastrointestinal	Avastin, Tarceva, Xeloda	Avastin, Herceptin, Xeloda, Hedgehog Pathway Inhibitor
Breast	Avastin, Herceptin, Xeloda	Avastin, pertuzumab, T-DM1, Xeloda, PI3 Kinase
Lung	Avastin, Tarceva	Avastin, Tarceva, PI3 Kinase, MetMAb
Hematological	MabThera/Rituxan	Avastin, MabThera/Rituxan, GA101, ABT-263
Genito-urinary	Avastin	Avastin, Hedgehog Pathway Inhibitor
Skin & Soft Tissue		Hedgehog Pathway Inhibitor, PLX4032 (B-raf inhibitor), Avastin
Brain	Avastin	Avastin

Avastin potential for additional indications

Important Phase III news flow over next 2 years

Indication	Study name	Status	Regulatory Submission
2L HER2- mBC	**RIBBON-2**	Study met its primary endpoint. Data presented at SABCS	2010
Adjuvant CC	**AVANT**	Expect data 2010; event-driven	2010 (TBD)
1L metastatic ovarian cancer	**GOG-0218**	Top-line data announced Q1 2010	2010
	ICON-7	Expect data 2010 *(supportive study)*	2010
Relapsed platinum-sensitive ovarian cancer	**OCEANS**	Expect data 2010	2011
	GOG-0213	Expect data 2013	Non-registrational
1L hormone-refractory prostate cancer	**CALGB 90401**	Event driven study, expect data 2010	2011
1L HER2+ mBC	**AVEREL** *(combo with Herceptin)*	Expect data 2011	2011

Avastin Phase III GOG-218 Ovarian Cancer Study

Demonstrated PFS in the Maintenance Setting

Newly diagnosed advanced ovarian cancer

N=1,873

ARM A	ARM B	ARM C
Carboplatin + Paclitaxel X 6	Carboplatin + Paclitaxel X 6	Carboplatin + Paclitaxel X 6
Placebo every 21 days	Bevacizumab 15 mg/kg every 21 days 5-6 cycles followed by placebo for maximum of 15 months	Bevacizumab 15 mg/kg
for 15 months total		every 21 days for 15 months

Primary endpoint: Progression-free survival

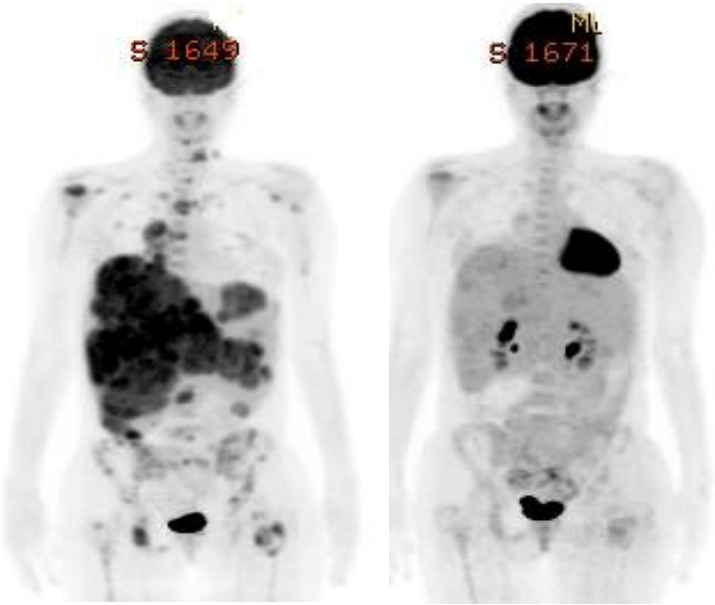
Secondary endpoint: Overall survival

- The study met its primary endpoint by showing that maintenance use of Avastin, following Avastin plus chemotherapy, increased the time women with previously untreated advanced ovarian cancer lived without the disease worsening, compared to chemotherapy alone.
  - Data to be presented at ASCO, June 2010
  - Expect ICON-7 (supportive study) data in 2010
- Expect OCEANS data in 2011 (relapsed platinum-sensitive ovarian cancer)

BRAF inhibitor (RG7204) in melanoma

Early results are promising

- **Results presented at ECCO/ESMO from Phase I studies in patients with BRAF^{V600} mutated, refractory metastatic melanoma have shown impressive clinical benefit**
  - 60–70% response rate
  - Rapid symptom improvement in some patients
- **Common toxicities: arthralgias, rash, photosensitivity, fatigue**
- **SCC of skin (Kerathoacanthoma type) observed in ~25% of patients, treated by excision**



Baseline Day 15

PET Scan

BRAF Inhibitor (RG7204) Development Program

Potential for first and best in class

Patient Population	Solid Tumors	Previously Treated Metastatic Melanoma BRAF mutation positive	Previously Untreated Metastatic Melanoma BRAF mutation positive
Phase/Study	**Phase I**	**Phase II BRIM2**	**Phase III BRIM3**
# of Patients	N=~100	N=~90	N=680
Design	• Dose escalation study	• Single ARM: RG7204	• ARM A: RG7204 • ARM B: dacarbazine
Primary Endpoint		• Best overall response rate assessed by IRC using RECIST criteria	• Overall survival
Status	• Phase I data presented at ASCO 2009 • BRAF mutation-positive metastatic melanoma extension cohort data presented at ECCO/ESMO 2009 • Extension cohort in BRAF mutation-positive metastatic colorectal cancer completed enrolment Q4 2009	• FPI Q3 2009	• FPI Q1 2010

In collaboration with Plexxikon

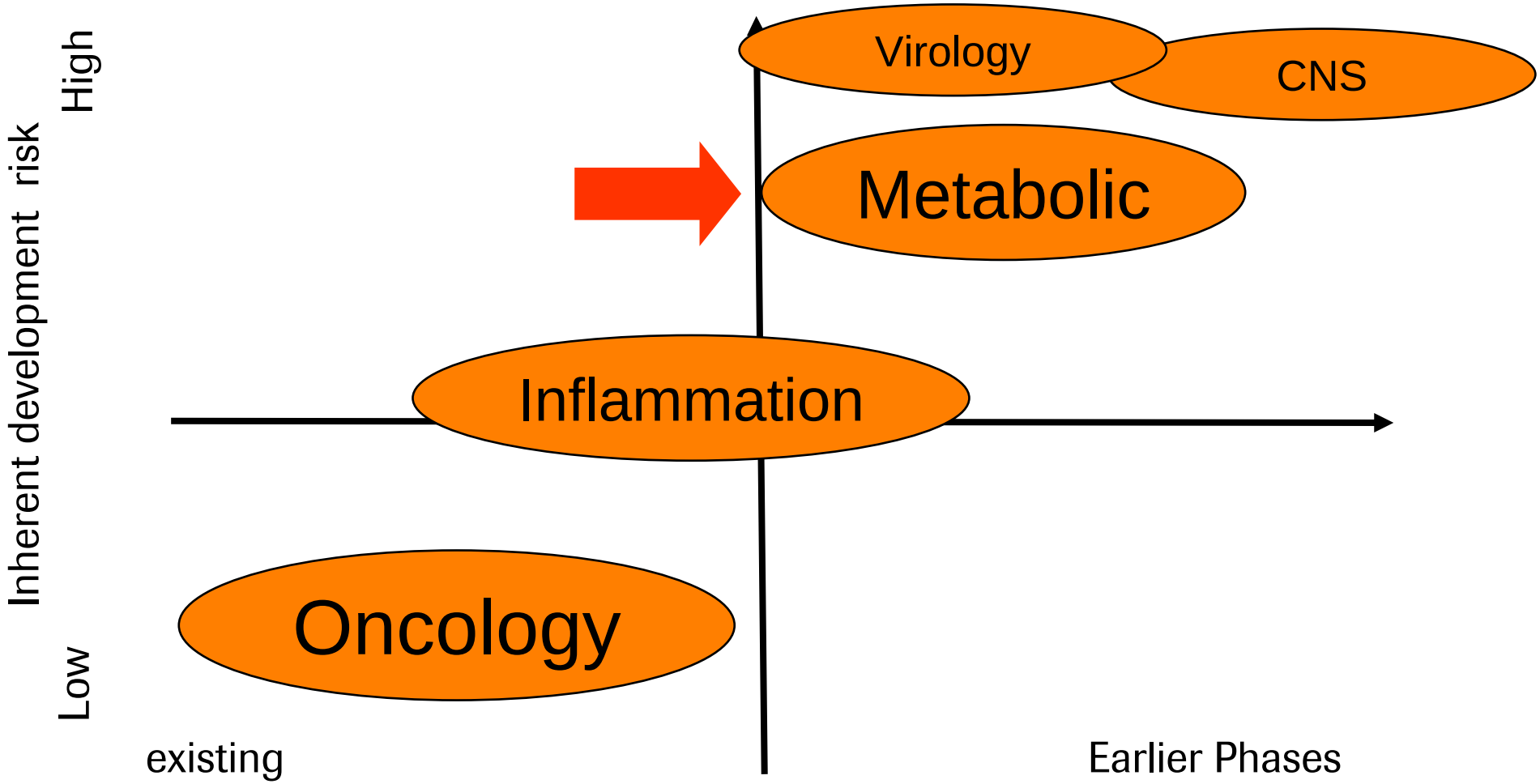
Pending Oncology Regulatory Submissions

Fuel for Growth in Near Future

Product	Indication	Study	Region	Status
Avastin	1st line mBC, combo with standard chemo	**RIBBON-1 & AVADO**	US	PDUFA Sept. 17th
Avastin	1st line mBC, combo with standard chemo	**RIBBON-1**	EU	EMEA submission Q4 2009
Rituxan	CLL 1st line	**CLL-8**	US	FDA approval Q1 2010 ✔
Rituxan	CLL relapsed	**REACH**	US	FDA approval Q1 2010 ✔
Herceptin	HER2+ gastric cancer	**ToGA**	EU	EMEA approval Q1 2010 ✔
Tarceva	1st line maint. NSCLC	**SATURN**	US, EU	PDUFA April 18th
Xeloda	Adjuvant CC; combo with oxaliplatin	**XELOXA (NO16968)**	EU	EMEA submission Q4 2009; positive CHMP opinion Q1 2010

Key drivers for long term development in place

Develop the short-term drivers while not neglecting the long-term



ILLUSTRATIVE

Why are we developing Taspoglutide?

- **Five positive phase 3 trials (approx. 4,000 patients) – remarkably consistent and robust data at 6 months**
  - potent A1c reduction, including patients with low baseline A1c and versus clinically relevant dose of Lantus
  - weight loss
  - Manageable GI adverse events resulting in a low discontinuation rate
  - No incremental hypoglycemia
- **Patient friendly delivery system for launch**
  - Ready-to-use, disposable, pre-filled syringe, staked-in-needle (29 gauge)
  - Used in phase 3 program
- **Results of cacinogenicity studies support the ongoing clinical development of Taspoglutide**

Taspoglutide: T-emerge Positive Phase III study results to date

Study	Description	Headline Results
T·emerge 1	Monotherapy	**Primary endpoint met:** superior HbA1c reduction versus placebo
T·emerge 2	H2H vs. Byetta	**Primary endpoint met:** significant superiority on HbA1c versus twice-daily exenatide
T·emerge 4	H2H vs. Januvia vs. placebo	**Primary endpoint met:** superiority in HbA1c reduction versus sitagliptin.
T·emerge 5	H2H vs. Lantus	**Primary endpoint met:** non-inferiority in HbA1c change versus insulin glargine
T·emerge 7	Obese T2DM patients	**Primary endpoint met:** HbA1c superiority versus placebo in patients with high BMI

Taspoglutide

A potentially best-in-class GLP-1 analogue

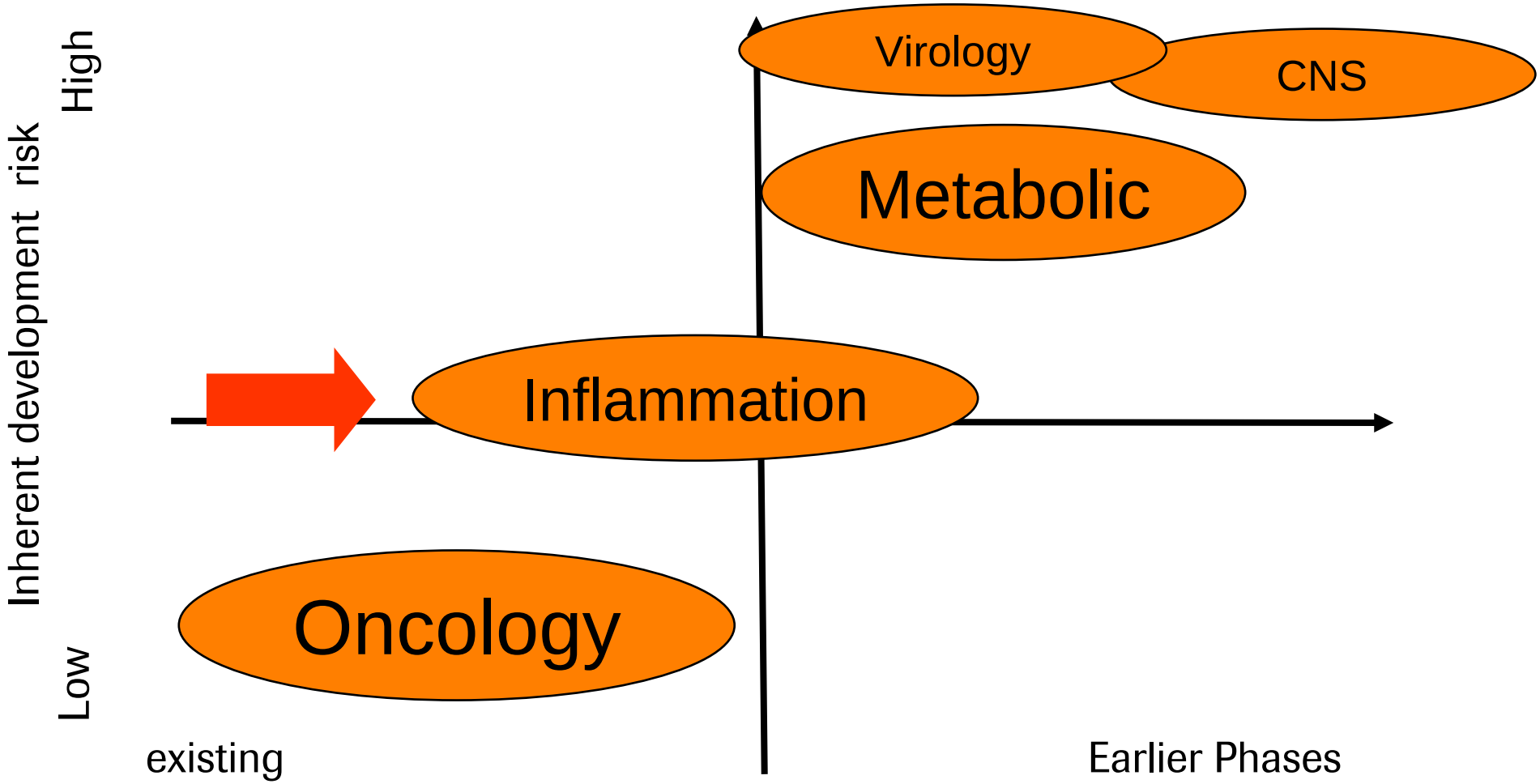
- Anticipate regulatory submissions in 2011

Type 2 Diabetes								
Patient Population	**Diet and Exercise Failures**	**Metformin, TZD, or Metformin + TZD Faliures**	**Pioglitazone + Metformin Failures**	**Metformin Failures**	**Metformin + SU Failures**	**SU ± Metformin Failures**	**Patients with high BMI**	**History of Cardiovascular Events**
Phase/ Study	**Phase III T-emerge 1**	**Phase III T-emerge 2**	**Phase III T-emerge 3**	**Phase III T-emerge 4**	**Phase III T-emerge 5**	**Phase III T-emerge 6**	**Phase III T-emerge 7**	**Phase III T-emerge 8** *Prospective Study*
# of Patients	N=373	N=1,189	N=330	N=636	N=1,049	N=650	N=305	N=2,000
Design	• **ARM A**: Taspoglutide 10mg • **ARM B:** Taspoglutide 20mg • **ARM C:** Placebo	• **ARM A:** Taspoglutide 10mg • **ARM B:** Taspoglutide 20mg • **ARM C:** Exenatide BID	• Taspoglutide vs. placebo	• **ARM A:** Taspoglutide 10mg • **ARM B:** Taspoglutide 20mg • **ARM C:** Sitagliptin • **ARM D:** Placebo	• **ARM A:** Taspoglutide 10mg • **ARM B:** Taspoglutide 20mg • **ARM C:** Insulin glargine	• Taspoglutide vs. pioglitazone	• **ARM A:** Taspoglutide 20mg + metformin • **ARM B:** Placebo	• **ARM A**: Taspoglutide + SOC • **ARM B:** Placebo + SOC
Primary Endpoint	• Absolute change from baseline in HbA1c	• Absolute change from baseline in HbA1c	• Absolute change from baseline in HbA1c	• Absolute change from baseline in HbA1c	• Absolute change from baseline in HbA1c	• Absolute change from baseline in HbA1c	• Absolute change from baseline in HbA1c	• Composite cardiovascular endpoint
Status	• Study met its primary endpoint Q4 2009 • Data submitted for presentation at ADA 2010	• Study met its primary endpoint Q4 2009 • Data submitted for presentation at ADA 2010	• Enrolment completed Q4 2009	• Study met its primary endpoint Q4 2009 • Data submitted for presentation at ADA 2010	• Study met its primary endpoint Q4 2009 • Data submitted for presentation at ADA 2010	• Enrolment completed Q4 2009	• Recruitment completed • Data submitted for presentation at ADA 2010	• FPI Q1 2010

In-licensed from Ipsen
TZD = Thiazolidinedione; BMI = Body Mass Index; SOC = Standard of Care.

Key drivers for long term development in place

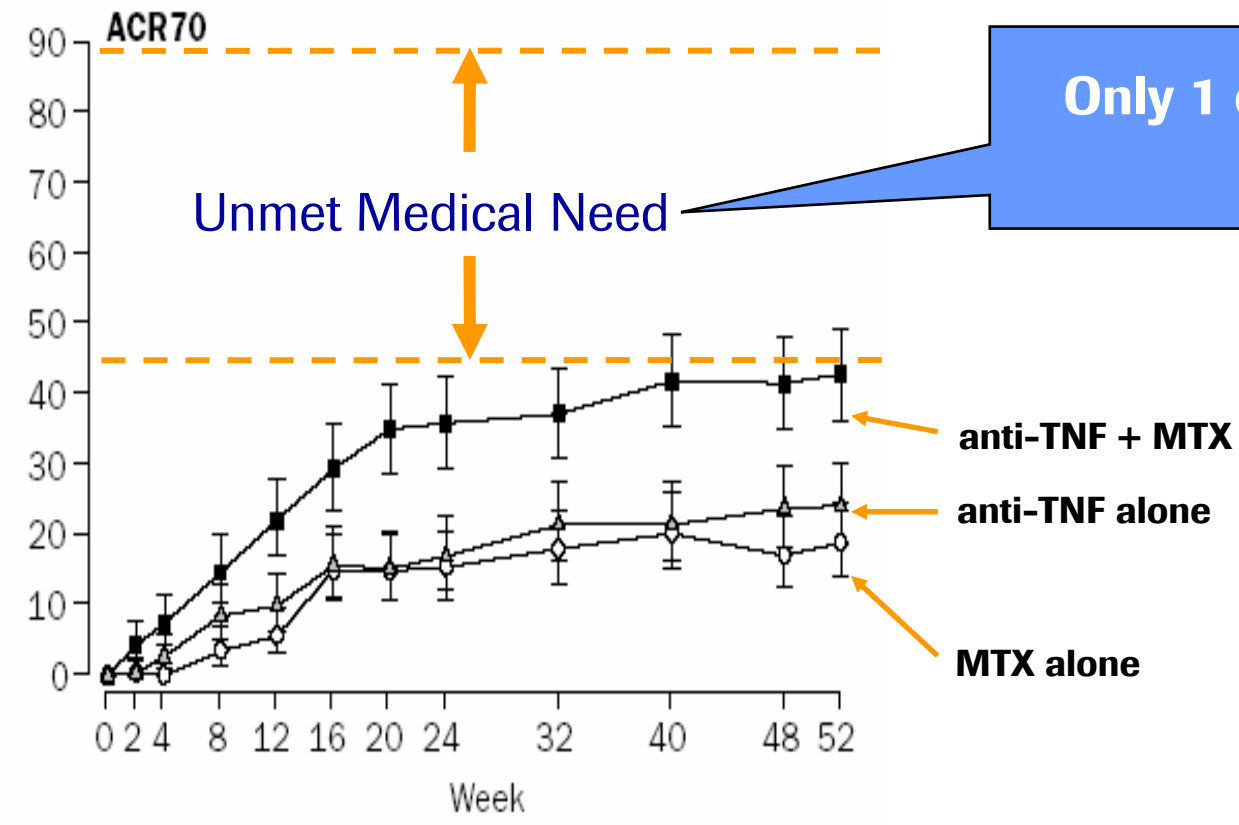
Develop the short-term drivers while not neglecting the long-term



ILLUSTRATIVE

Rheumatoid Arthritis: Not all patients respond to current therapy

Gold standard therapy
anti-TNF + MTX



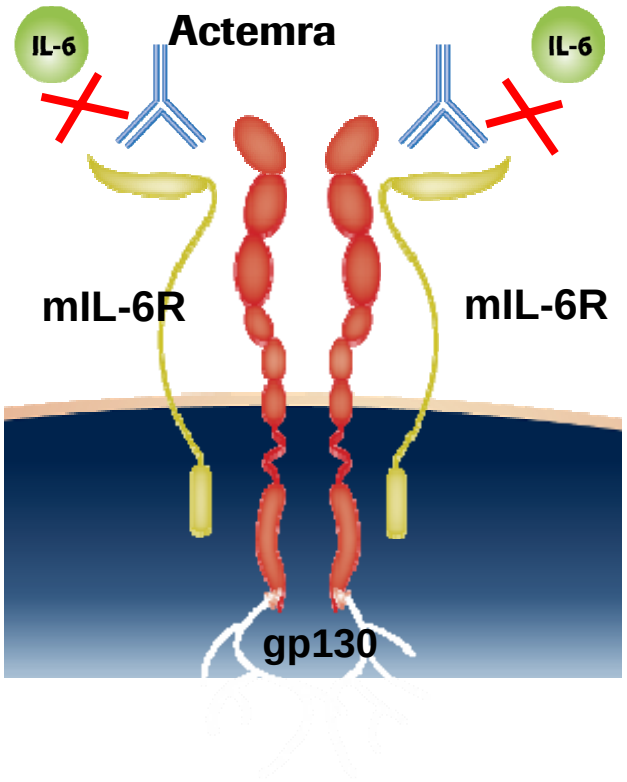
Only 1 of 3 patients receives significant benefit

ACR 70=70% Improvement in:

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

Actemra: first biologic to inhibit IL-6 receptor

Consistently high and durable remission rates - across all disease stages



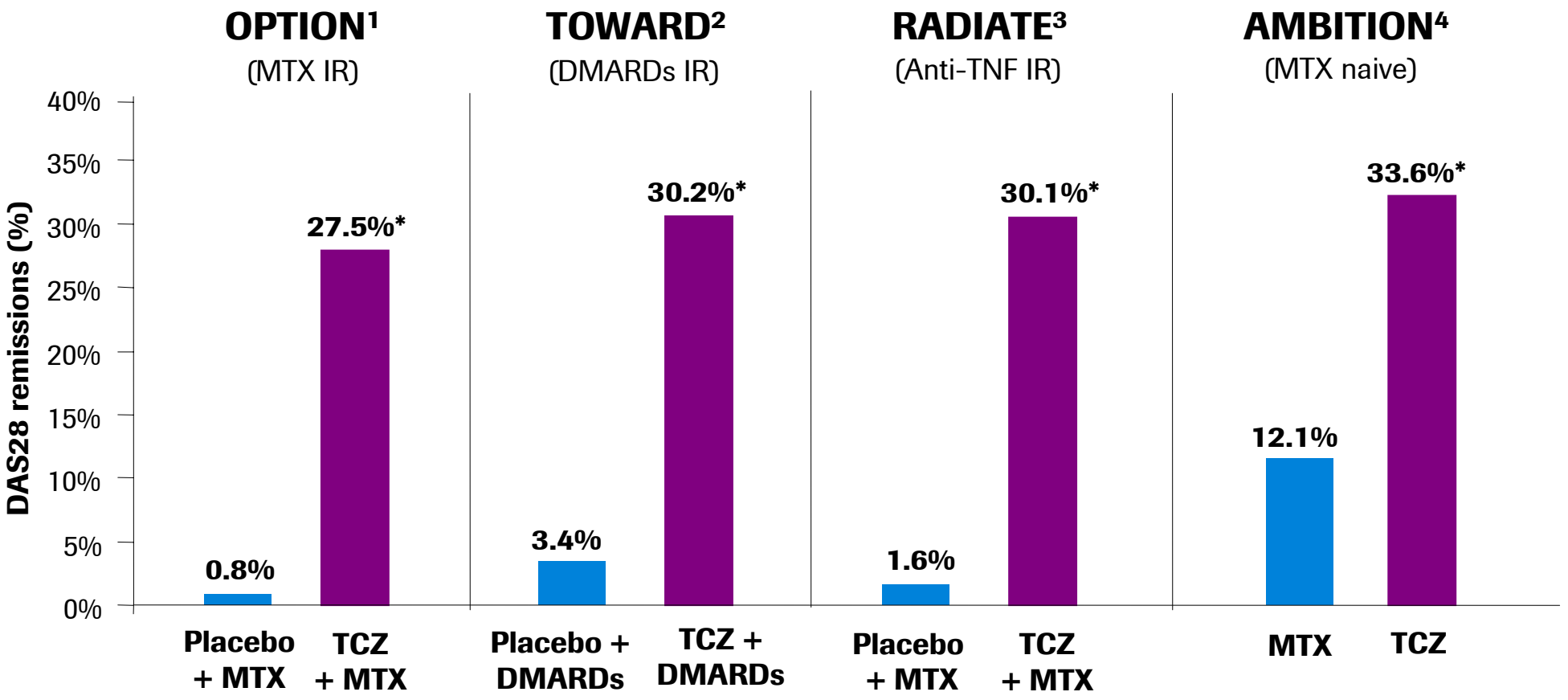
- **Unique MOA**
  - IL-6 is the most abundant cytokine in the rheumatoid synovium
  - IL-6 plays a role in local and systemic inflammation associated with RA
- **Strong efficacy data:**
  - Consistently high remission rates across patient types[1]
  - Only biologic to have demonstrated superiority over methotrexate as monotherapy[2]
  - Unique combination of rapid onset of action and efficacy that keeps improving over time
  - Safety profile has been well characterised in the most comprehensive Phase III program for any RA biologic

1 Seminars in Arthritis & Rheumatism: In Press

2 Jones et al., EULAR 2009, Abstract FRI0252

Actemra phase III trials: unsurpassed efficacy

Around 30% of patients achieved DAS28 remission at week 24 – regardless of concomitant or prior therapy



[1] Smolen JS, et al. Lancet 2008,371,987-97

[2] Genovese et al., Athrisits & Rheumatism, vol 58, no 10, 2008, 2968-2980

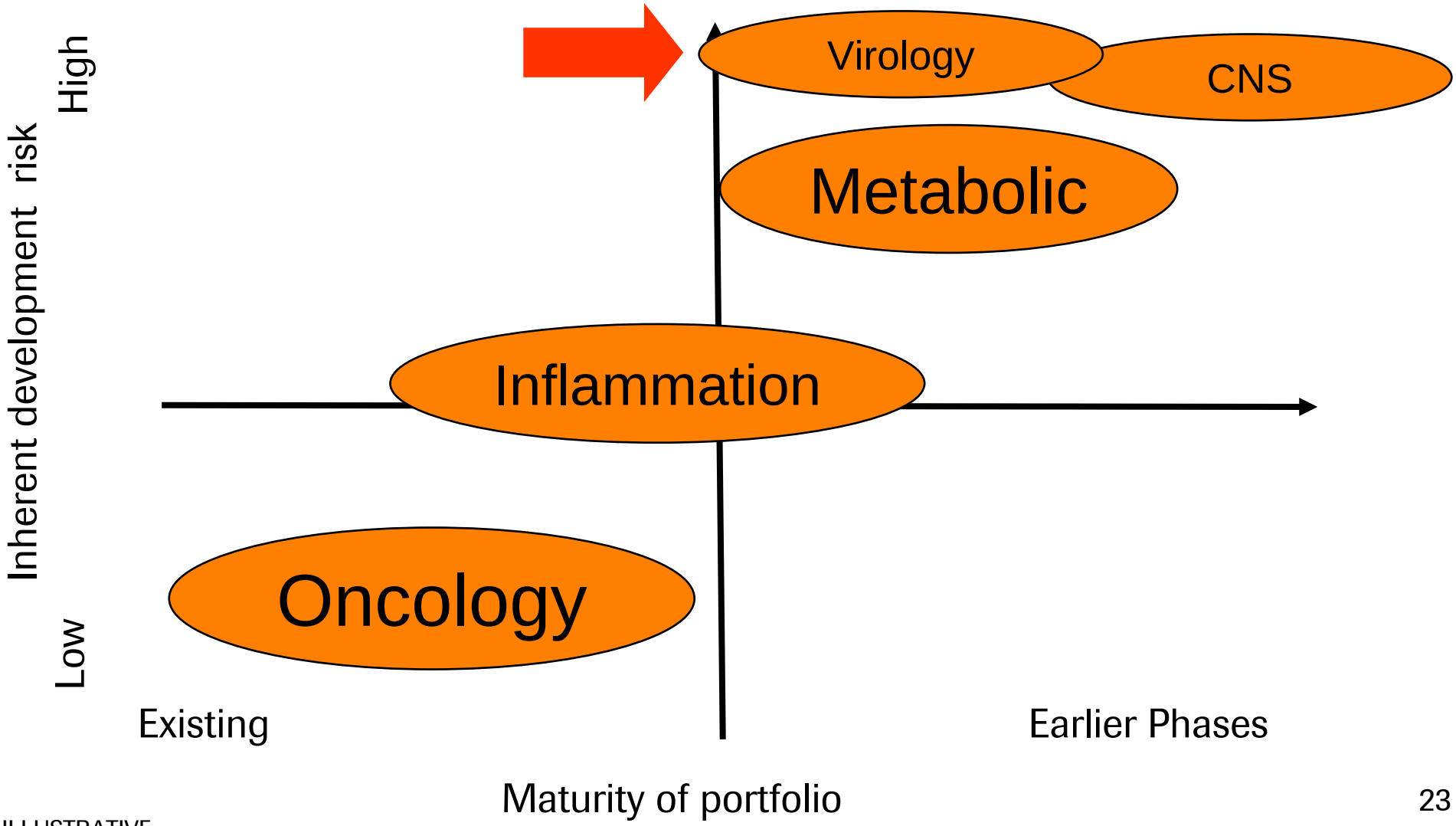
[3] Emery et al., Ann Rheum DIs 2008, 67,1516-1523

[4] Jones et al., Ann Rheum Dis 2009, Mar 17

* p ≤0.0001; TCZ dose 8 mg/kg

Key drivers for long term development in place

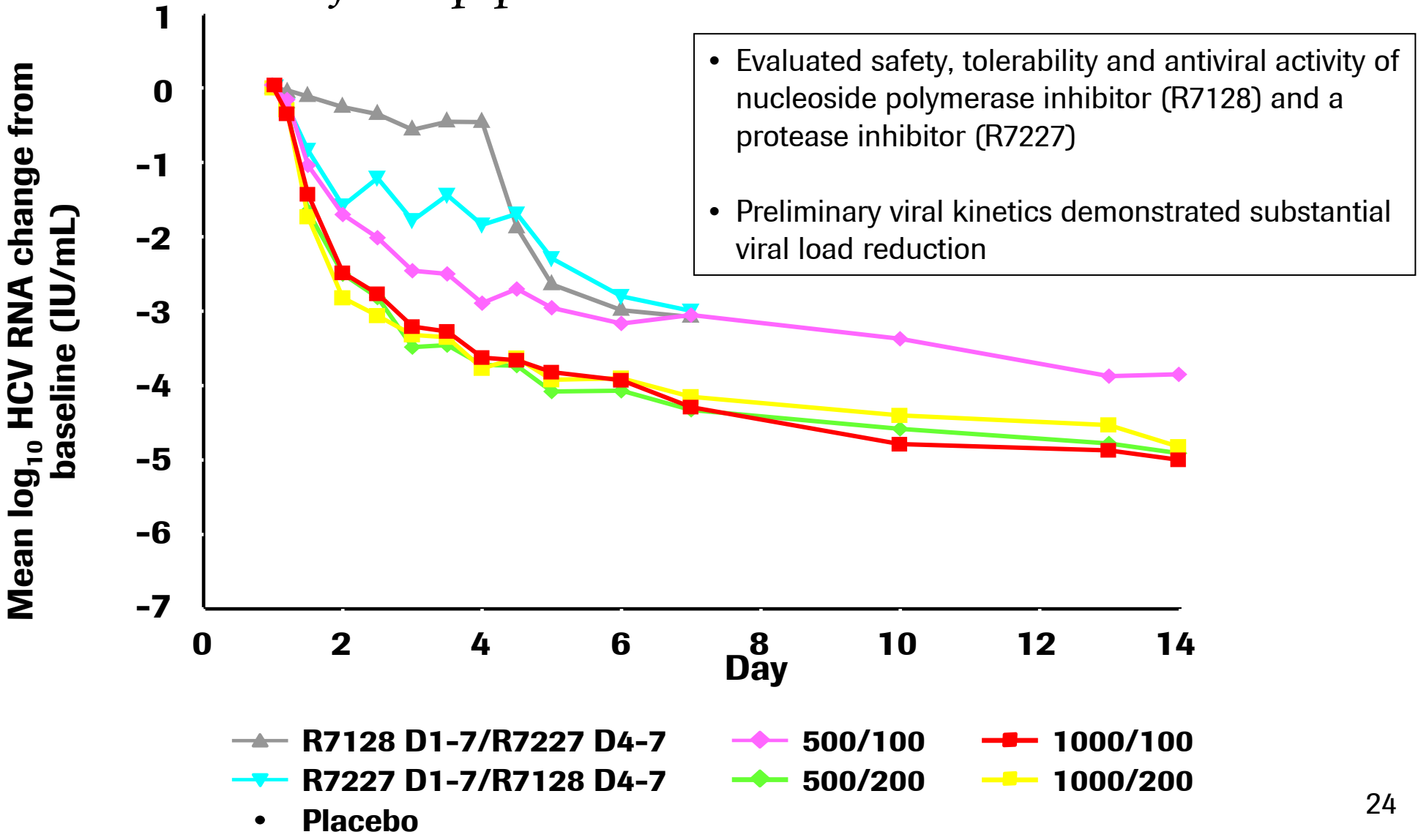
Develop the short-term drivers while not neglecting the long-term



ILLUSTRATIVE

INFORM-1 Study

Combination of two pipeline molecules to treat HCV



- Evaluated safety, tolerability and antiviral activity of nucleoside polymerase inhibitor (R7128) and a protease inhibitor (R7227)
- Preliminary viral kinetics demonstrated substantial viral load reduction

INFORM-1 study conclusions

- The orally administered combination[1] of R7128 and R7227 demonstrated
  - Significant antiviral potency
  - Sustained viral suppression
  - Acceptable safety and tolerability

- For the first time two oral direct-acting antivirals can be safely combined in HCV patients

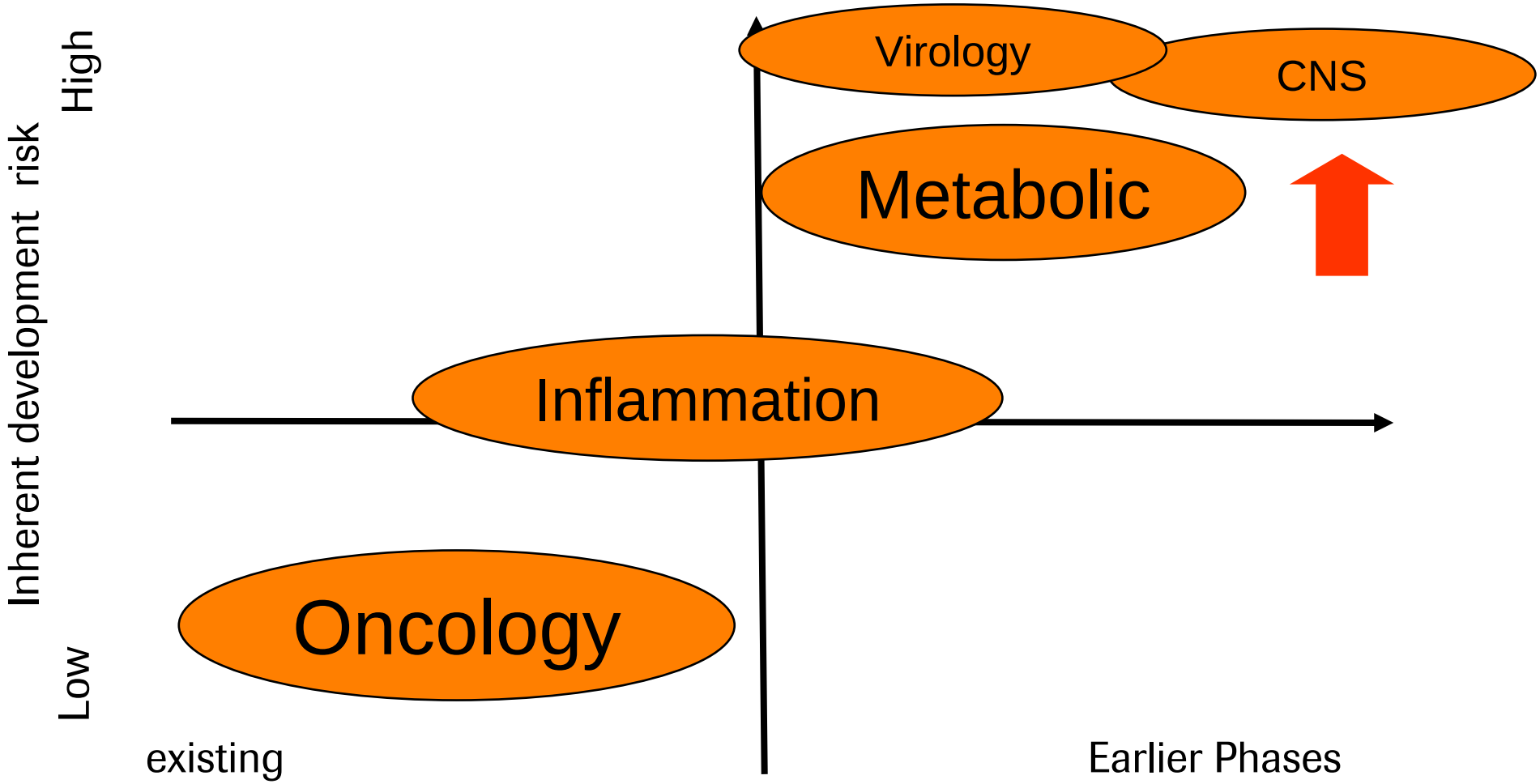
- This combination of a potent protease and nucleoside polymerase inhibitor may represent a future treatment regimen either with or without Peg-IFN plus ribavirin

Phase IIb INFORM-3 plans underway

1 Over a 14 days treatment

Key drivers for long term development in place

Develop the short-term drivers while not neglecting the long-term



ILLUSTRATIVE

Attractiveness of CNS Segments

Driven by market opportunity and scientific feasibility

High Priority

- ❑ Alzheimer's disease
- ❑ Schizophrenia
- ❑ Treatment-resistant depression (TRD)
- ❑ Neurodegenerative disorders*

Opportunistic

- ❑ Multiple sclerosis
- ❑ Neuropathic pain
- ❑ Attention-Deficit Hyperactivity Disorder
- ❑ Depression – inadequate responder to SSRI
- ❑ Autism
- ❑ Bipolar disorders

Low Priority

- ❑ Anxiety disorders
- ❑ Sleep disorders
- ❑ Migraine
- ❑ Epilepsy
- ❑ Stroke

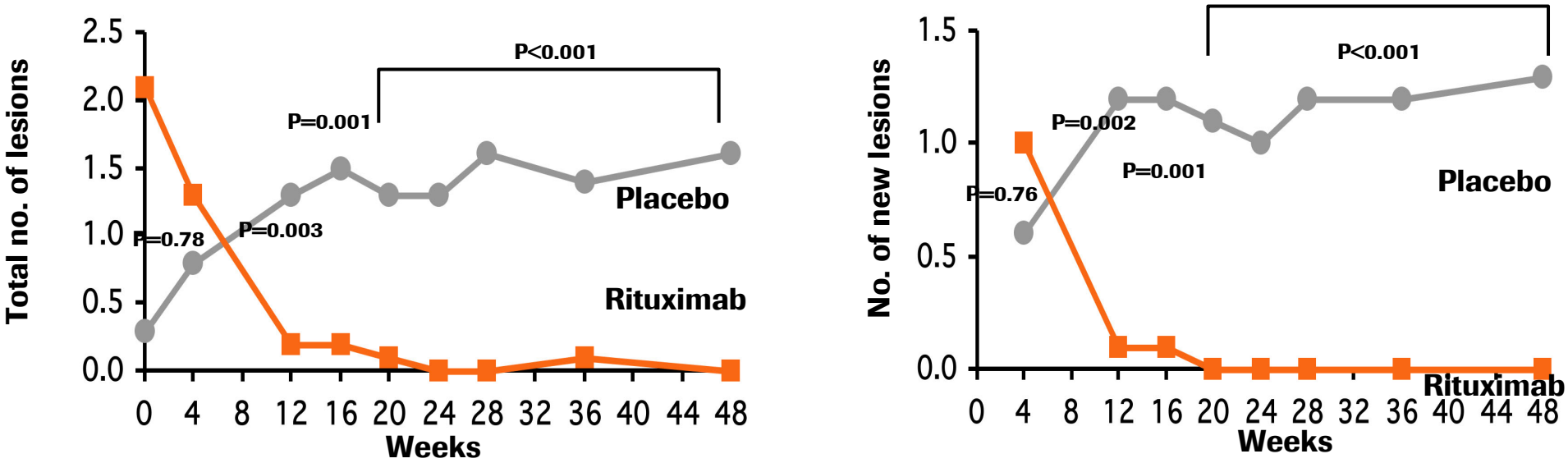
* Other neurodegenerative disorders includes Amyotrophic Lateral Sclerosis (ALS), Parkinson's Disease (PD)

Relapsing-Remitting Multiple Sclerosis

The Role of B Cells

B-Cell Depletion with Rituximab in Relapsing-Remitting Multiple Sclerosis

Stephen L. Hauser, M.D.,et al



Gadolinium-Enhancing Lesions in Each Study Group from Baseline to Week 48.

Panel A: mean total number of gadolinium-enhancing lesions by week
Panel B: mean number of new gadolinium-enhancing lesions by week.

Phase II Ocrelizumab RRMS study met its primary endpoint. Full results to be presented at an upcoming medical meeting.

15 major positive phase III outcomes in 2009

Fuel for growth

	Product	Indication	Study	Global peak sales potential
Oncology	MabThera/Rituxan	iNHL 1st line maintenance	PRIMA	●●
	Avastin	2nd line mBC	RIBBON-2	●●
	Xeloda	Adj colon cancer	NO16968	●
	Herceptin	HER2-positive gastric cancer	ToGA	●●
	Tarceva	NSCLC 1st line maintenance	SATURN (final OS data)	●
	Tarceva+Avastin	NSCLC 1st line maintenance	ATLAS	●
Inflammation	Actemra	RA (progression of joint damage)	LiTHE 2 years	●●●
	Actemra	sJIA	TENDER	●
Ophthalmology	Lucentis	RVO	BRAVO and CRUISE	●
Metabolism	taspoglutide	Type 2 diabetes	T-emerge 1, 2, 4, 5, 7	●●●

●< CHF 500 mn; ●● CHF 0.5 to 1 bn; ●●● CHF 1 bn

We Innovate Healthcare

Key Data Results in 2010

- **Oncology**
  - Avastin Phase III **CALGB 90401** in 1L hormone-refractory prostate cancer
  - Avastin Phase III **AVANT** in adjuvant CC
  - ✓ Avastin Phase III **AVAGAST** in advanced gastric cancer *(negative)*
  - ✓ Avastin Phase III **GOG-218** in 1L ovarian cancer *(positive)*
  - Avastin Phase III **ICON-7** in 1L ovarian cancer
  - Avastin Phase III **OCEANS** in 2L ovarian cancer
  - T-DM1 + Pertuzumab interim Phase Ib/II in HER2+ mBC
  - Pertuzumab Phase II in neoadjuvant HER2+ BC **(NeoSphere)**
  - Xeloda Phase III in adjuvant BC **(NO17629)**

- **Immunology**
  - Orcelizumab Phase III **SCRIPT** for RA anti-TNF IR
  - Orcelizumab Phase III **FILM** for RA MTX-naïve

- **Metabolism**
  - Taspoglutide Phase III **T-emerge** 3 and 6 for T2D

As of February 24, 2010