Translating excellence in science into customer benefit – an update on CNS portfolio

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Performance update and strategy

Update on CNS portfolio

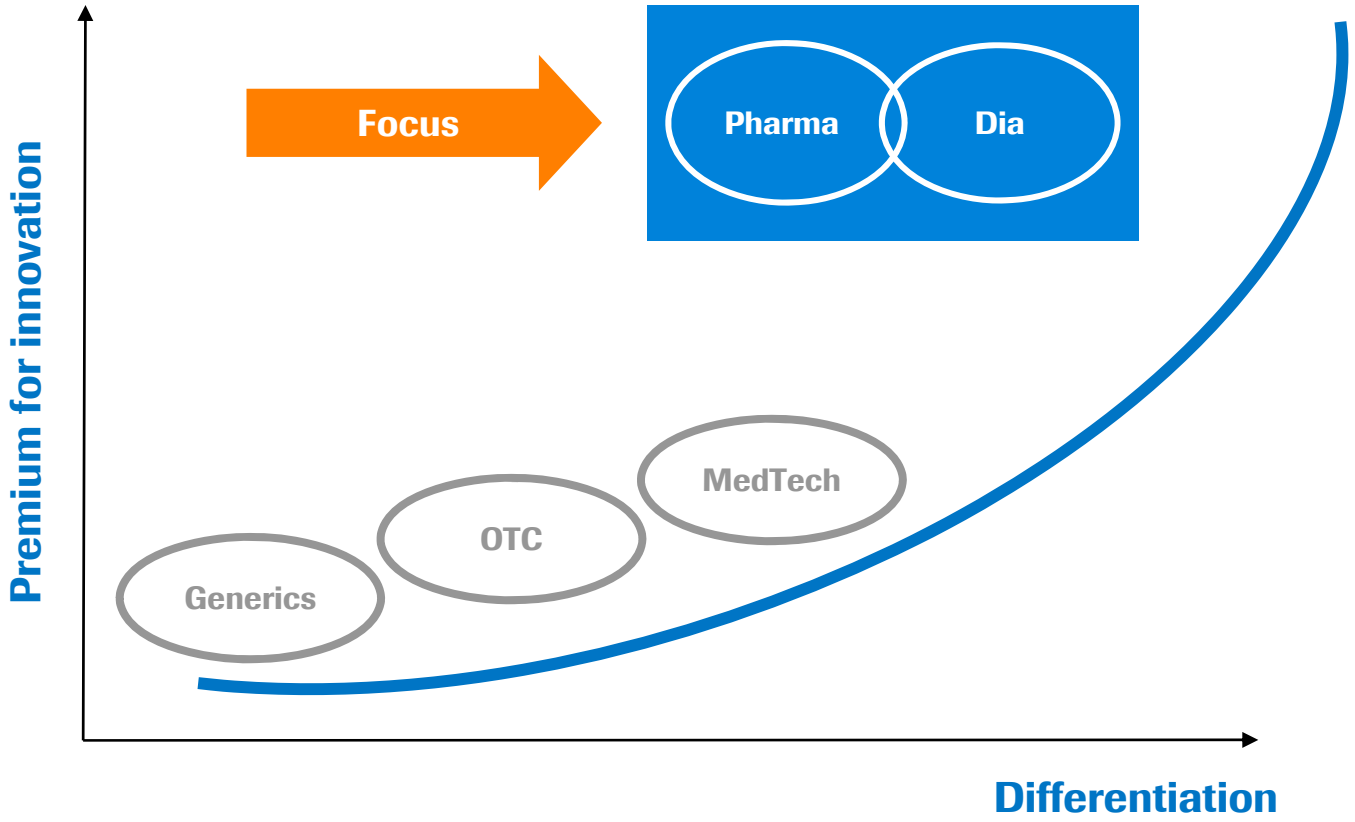
Q1 2011: Group sales

Supporting full-year guidance, strong currency impact

	2010 CHF m	2011 CHF m	change in % CHF	change in % local	Excluding Tamiflu[1]
Pharmaceuticals Division	**9,727**	**8,712**	**-10**	**-2**	**+1**
Diagnostics Division	**2,518**	**2,408**	**-4**	**+6**	**+6**
Roche Group	**12,245**	**11,120**	**-9**	**0**	**+2**

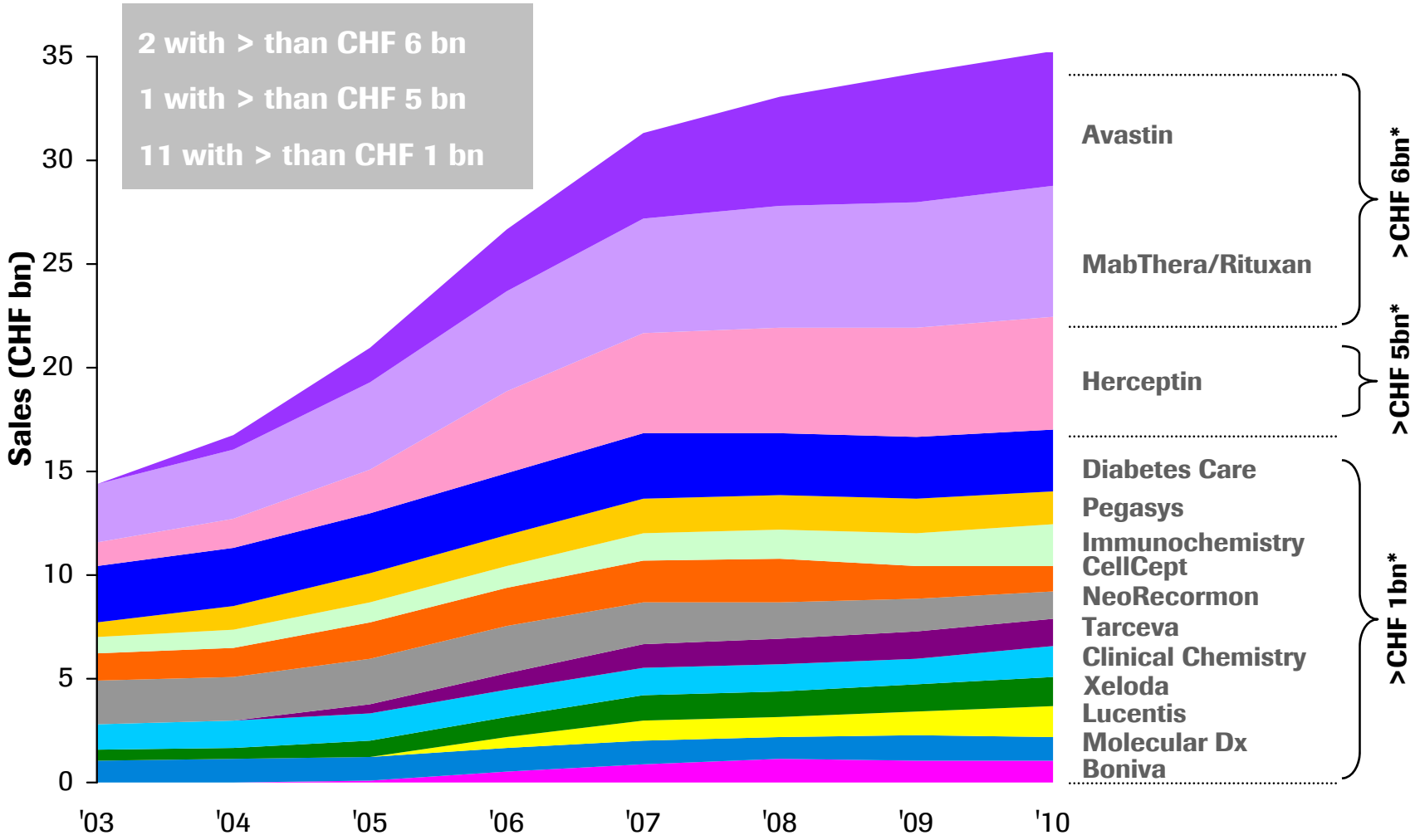
[1] local currency

Roche: Focused on medically differentiated therapies



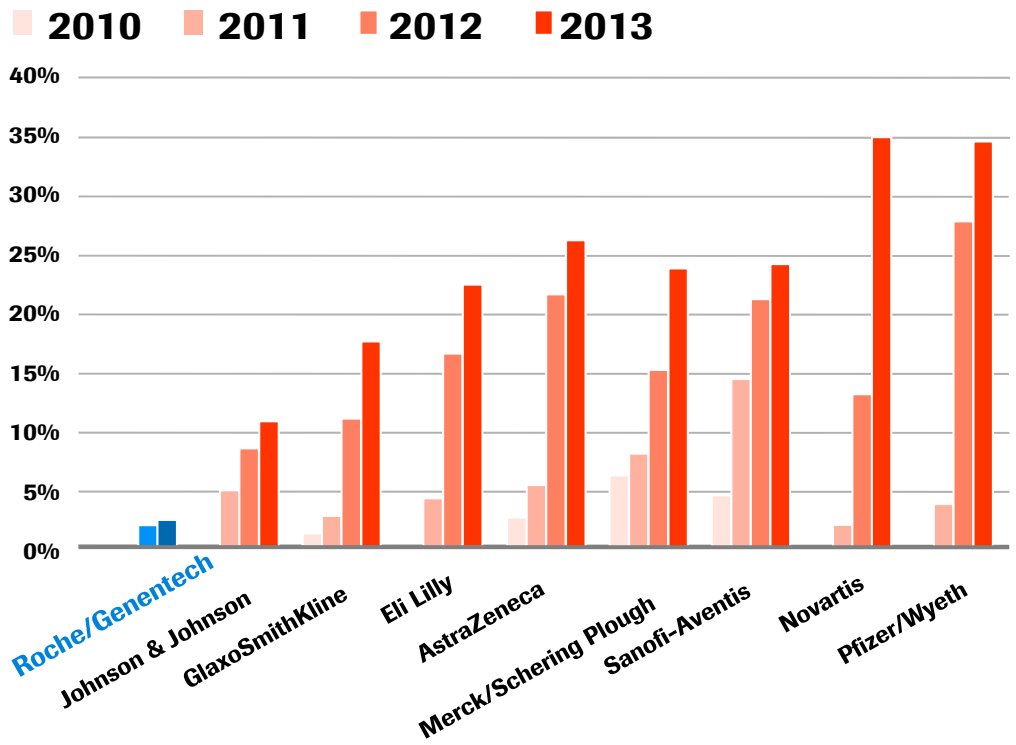
Key Pharmaceuticals & Diagnostics products

A risk-diversified portfolio of drugs and BUs



*** 2010 sales**

Roche: Limited exposure to patent expiries in the short and medium term



Business impact from biosimilars 2014/15 and beyond?

% Sales Lost calculated by subtracting given year sales ('10, '11, '12, '13) from full year sales from year prior to LOE.
Data excludes sales lost impact of products with LOE prior to 2010.
Source: Evaluate Pharma

Long patent protection
Biosimilars facing high hurdles

Long primary patent protection of our key biologics

Patents	US	EU ROW/EM
Avastin	2019	similar
Lucentis	2019	marketed by Novartis
Rituxan/ MabThera	2018	earlier
Herceptin	2019	earlier
Pegasys	2018	similar

Biosimilars outlook

US: recent healthcare legislation opens pathway for biosimilars

FDA in the process of developing guidelines

Data exclusivity for biologics 12 years

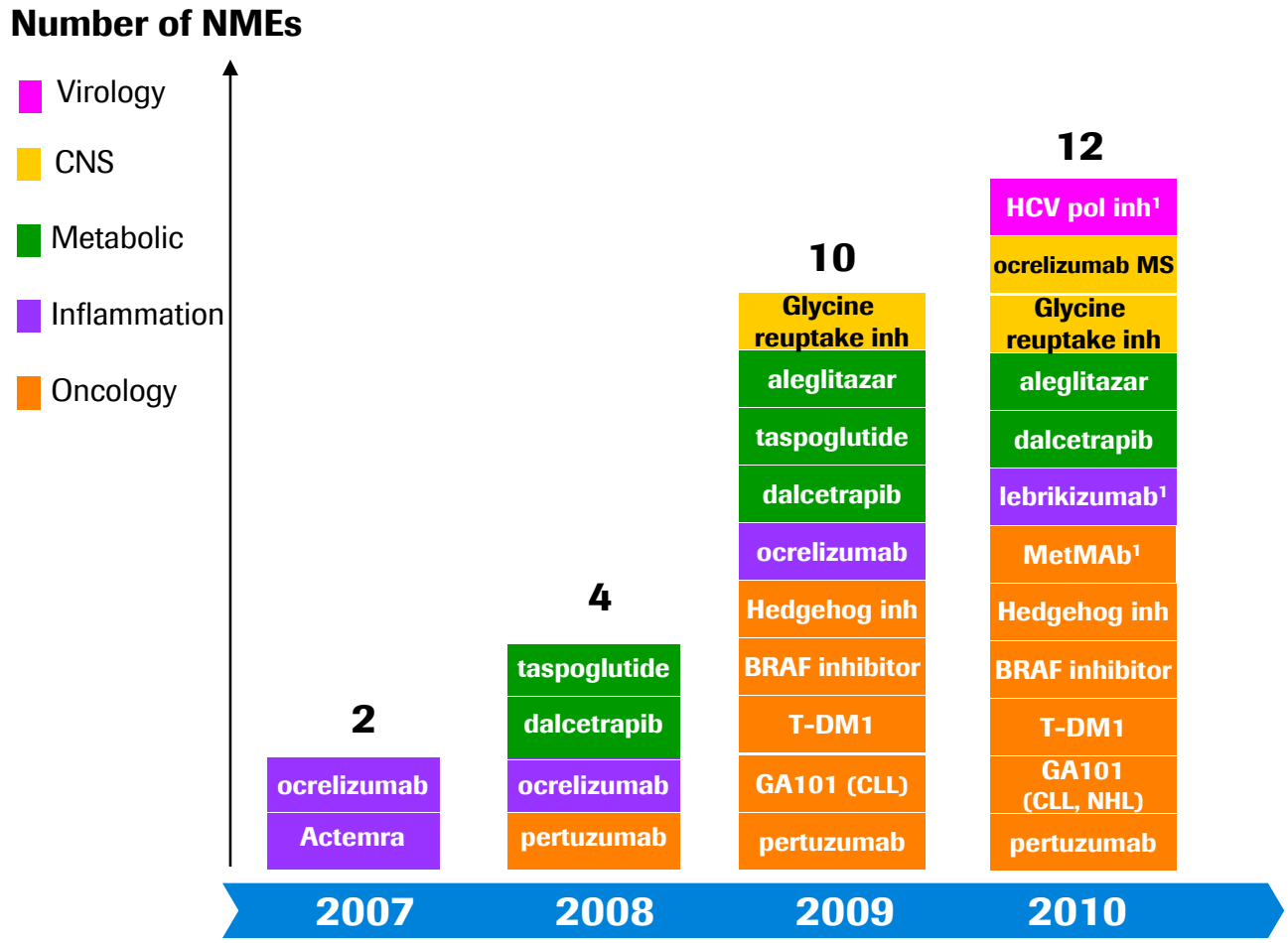
EU: legal and regulatory hurdles likely to remain high for biosimilars

ROW/EM: investment in countries with strong IP regulations (China)

Brand awareness important

A leading pipeline

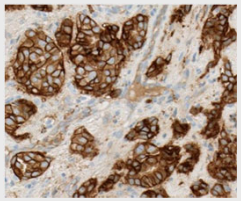
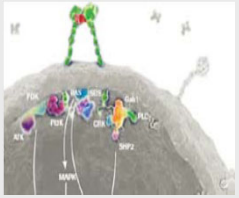
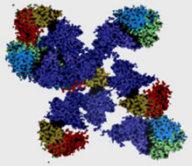
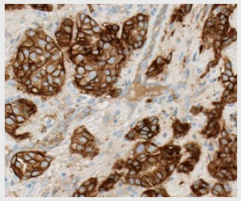
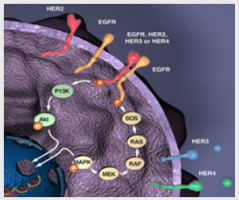
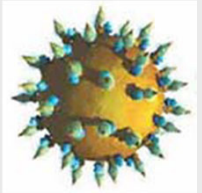
12 NMEs in late-stage development



[1] LIP decision made, phase III start pending

Creating medical value and improving patient care

Six NMEs in late-stage development have PHC approach

Diagnostics	 HER2/3 (Pertuzumab)	 Met (MetMAb)	 Periostin (lebrikizumab)
Companion Diagnostics	 HER2 (T-DM1)	 BRAF V600 (BRAF inh)	 HCV load, genotype (HCV pol inh)

NMEs = new molecular entities PHC = Personalised Healthcare

Not all products available in all countries; some products in development

We need to stay above industry success rates

Roche								
Success (+) Failure (-)	2008		2009		2010		2011 (Jan-Mar)	
	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)
Phase II	6		6		7		1	
Phase III	21	2	20	1	10	6	4	0
Total	27	2	26	1	17	6	5	0
Ph III success rate	91%		95%		62%		100%	

Industry ph III success rate	63%[1]	64%[2]

Based on IR up-dates

KMR Group, 1)= 2006-2008, 2)= 2007- 2009,

Key clinical trials since October 2010

18 positive studies in 6 months

Compound	Indication	Study
MetMAb	2nd/3rd line NSCLC	Randomised Phase II, ESMO 2010
Avastin	front line Ovarian Cancer	ICON7 Phase III, ESMO 2010
Ocrelizumab	RR Multiple Sclerosis	Randomised Phase II, ECTRIMS 2010
Mericitabine (RG7128)	Hepatitis C	PROPEL randomised Phase IIb, interim data AASLD 2010
Vemurafenib (BRAF inh)	Metastatic Melanoma	BRIM2 Phase II, Melanoma Research Congress 2010
GA101	Non-Hodgkin's Lymphoma	Randomised Phase II, ASH 2010
Glycine Reuptake inh. (GlyT-1)	Schizophrenia	Randomised Phase II, ACNP 2010
Pertuzumab	Neoadjuvant HER2+ Breast Cancer	NEOSPHERE randomised Phase II, SABCS 2010
Lebrikizumab	Asthma	Randomised Phase II, data in house
Dalcetrapib	CV risk reduction	DaI-VESSEL, DaI-PLAQUE safety data in house
T-DM1	1st line HER2-positive breast cancer	Randomised Phase II, Apr 2011
Vemurafenib (BRAF inh)	Metastatic Melanoma	BRIM3 Phase III interim analysis, Jan 2011
Tarceva	Advanced NSCLC	EURTAC Phase III interim analysis, Jan 2011
Avastin	Relapsed Ovarian Cancer	OCEANS Phase III, Feb 2011
Lucentis	Diabetic macular edema (DME)	RISE and RIDE, 2 Phase III studies, Feb-Mar 2011
Vismodegib (Hedgehog inh)	Basal Cell Carcinoma (mBCC)	Pivotal Phase II, Mar 2011

Pivotal studies in Q1 2011

Performance update and strategy

Update on CNS portfolio

The burden of brain disorders is one of the greatest challenges facing society today…

	Cause	YLD* millions
1	Unipolar depression	41.0
2	Refractive errors	14.0
3	Hearing loss, adult onset	13.3
4	Cataracts	9.9
5	Osteoarthritis	9.5
6	Schizophrenia	8.0
7	Anaemia	7.4
8	Bipolar Disorder	7.1
9	Birth asphyxia & birth trauma	6.9
10	Alzheimer & other dementia	5.8

*YLD: Years lived with disability

	Cause	Percent of total DALYs*
1	Unipolar depression	8.2
2	Ischemic heart disease	6.3
3	Cerebrovascular disease	3.9
4	Alzheimer & other dementias	3.6
5	Alcohol use disorders	3.4
6	Hearing loss, adult onset	3.4
7	COPD	3.0
8	Diabetes mellitus	3.0
9	Trachea, bronchus, lung cancers	3.0
10	Road traffic accidents	2.6

*DALYs: Years of life lost due to death and disability

WHO's Global Burden of Disease Report, 2004

… and yet commitment to the field is wavering

AstraZeneca drops psychiatric, other drug research

The decision to drop **psychiatry drug research** reflects the unpredictable and risky nature of clinical trials to assess medicines working on the brain, as well as a lack of good scientific opportunities, development head Anders Ekblom told Reuters.

LONDON, March 02, 2010 (Reuters)

Glaxo to Close Italy R&D Center

Feb. 5 -- GlaxoSmithKline Plc, the U.K.'s biggest drugmaker, plans to close a facility in Verona, Italy, affecting more than 500 research jobs, labor unions said.

Glaxo's northern Italian center, which specializes in **neuroscience research**, will be closed by the end of this year, the Filcem-Cgil, Femca-Cisl and Uilcem-Uil unions said in a joint e-mailed statement last night.

February 05, 2010 (Bloomberg)

Emerging knowledge of neurobiology opens new opportunities

Vision

Roche Neuroscience harnesses emerging science for serious patient needs

Strategy

- Focus on **serious conditions** with no approved, effective or safe treatments
- Deliver a differentiated portfolio by focusing on **mechanism-based** drug discovery
- Optimize benefit through **early intervention and personalized treatment**
- Understand the **needs of stakeholders:** patients, prescribers, regulators & payors

Therapeutic areas of focus

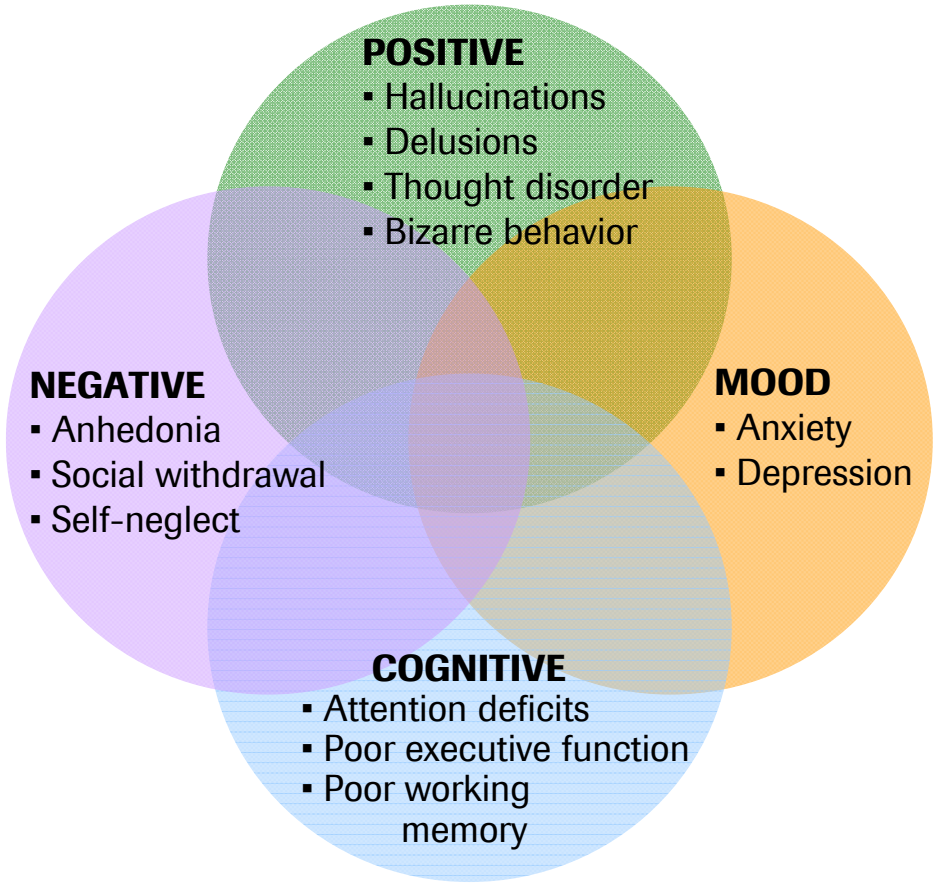
- Schizophrenia (negative and persistent symptoms)
- Depression (Treatment-Resistant Depression)
- Neurodevelopmental disorders (Fragile X, Down's, Autism)
- Neurodegeneration (Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis)

Glycine reuptake inhibitor (GlyT-1)

RG1678, the first GRI in schizophrenia

Schizophrenia
Disease and epidemiology

Multiple symptoms



Epidemiology*

Country	Diagnosed Prevalence (%)
US	0.7
Japan	0.8
France	0.7
Germany	0.8
Italy	0.8
Spain	0.7
UK	0.8

* Source: Decision Resources, Jan. 2010

Available treatment options

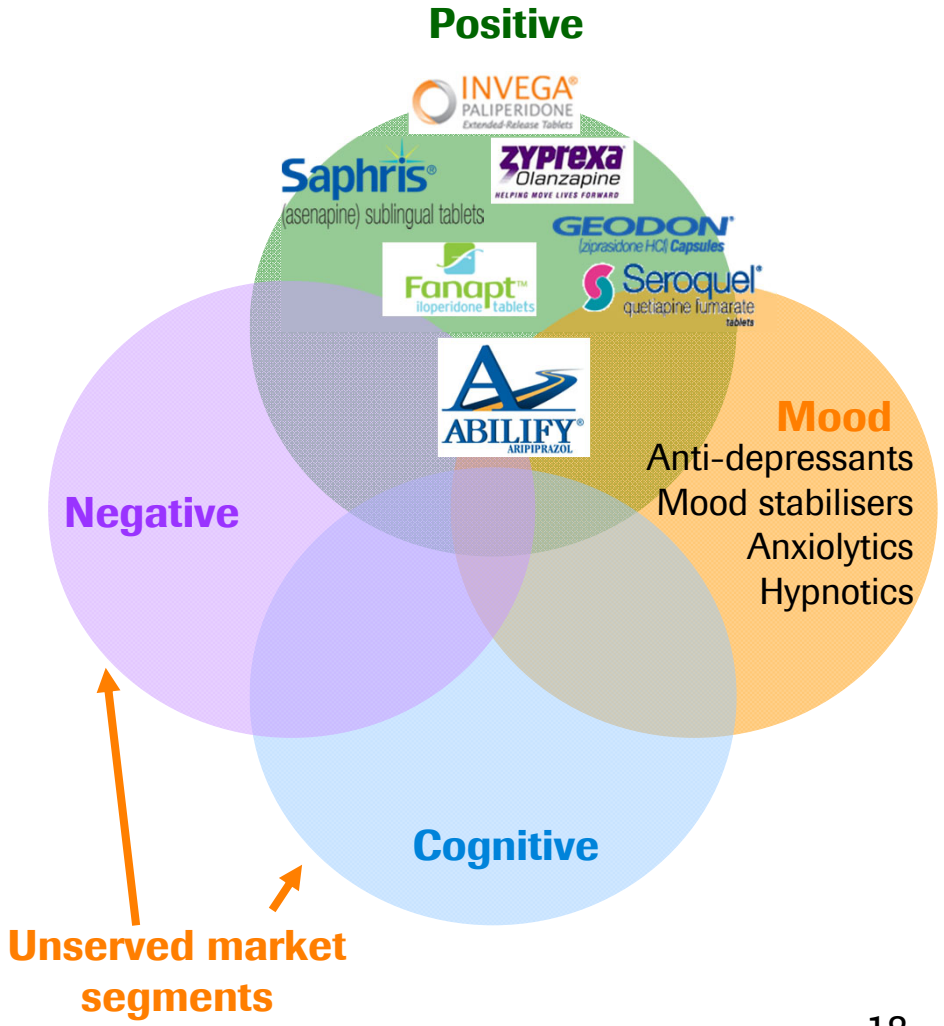
Only positive symptoms addressed by antipsychotics

Dual-dopamine/5HT2 antagonists:

- Poor efficacy in negative and cognitive symptoms
- Low tolerability: EPS (movement disorders), hypotension, obesity, diabetes, QTc prolongations

Better treatment for positive symptoms needed:

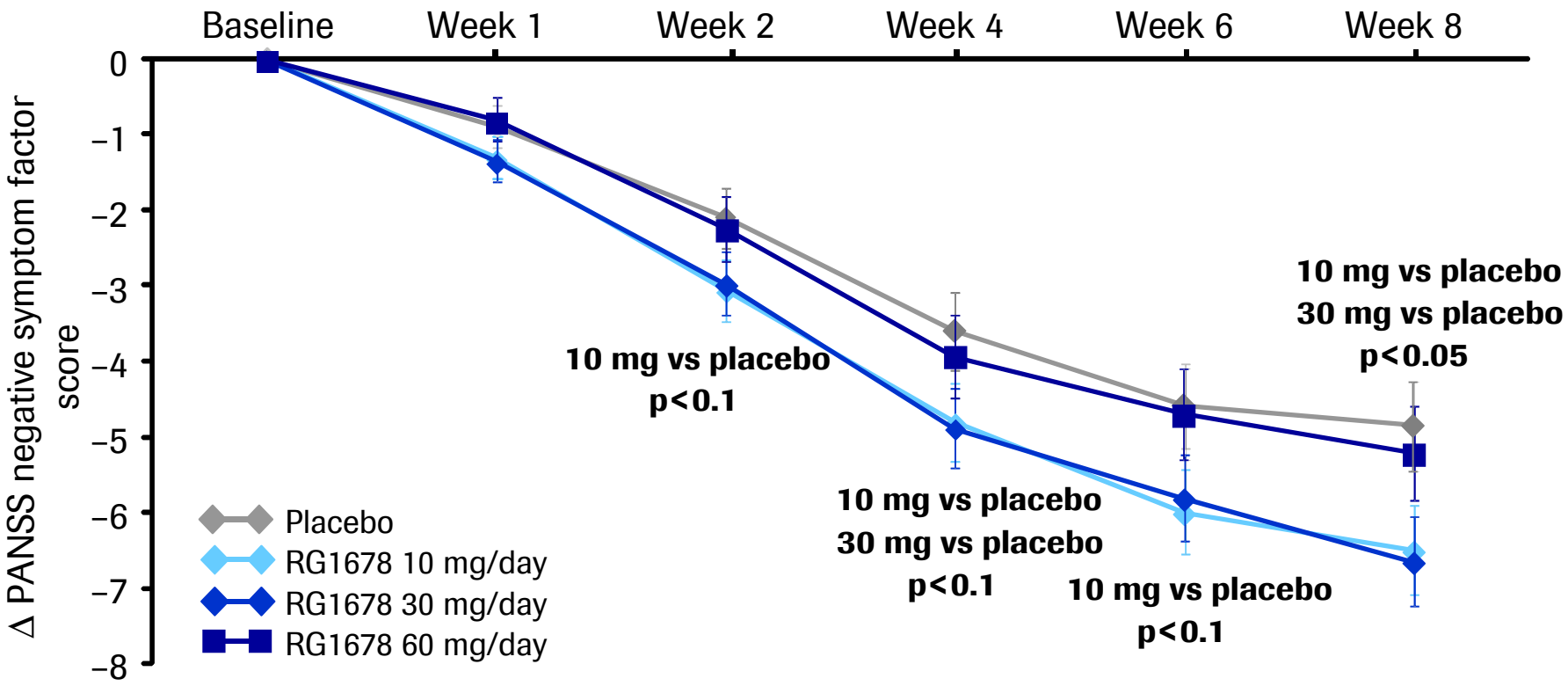
- Widespread use of combination therapy (app. 60 % *)
- No safety data for D2 combinations
- No controlled studies with combinations in schizophrenia



* Faries D, Ascher-Svanum H, Zhu B, Correll C, Kane J. BMC Psychiatry. 2005

GlyT-1 in negative symptoms of schizophrenia

*Significant reduction in negative symptom factor score**

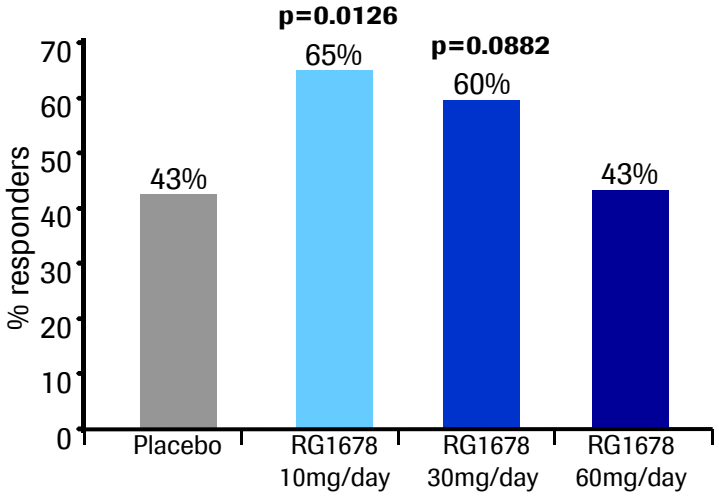


Effect Size (Week 8): 10 mg = 0.37, 30 mg = 0.40

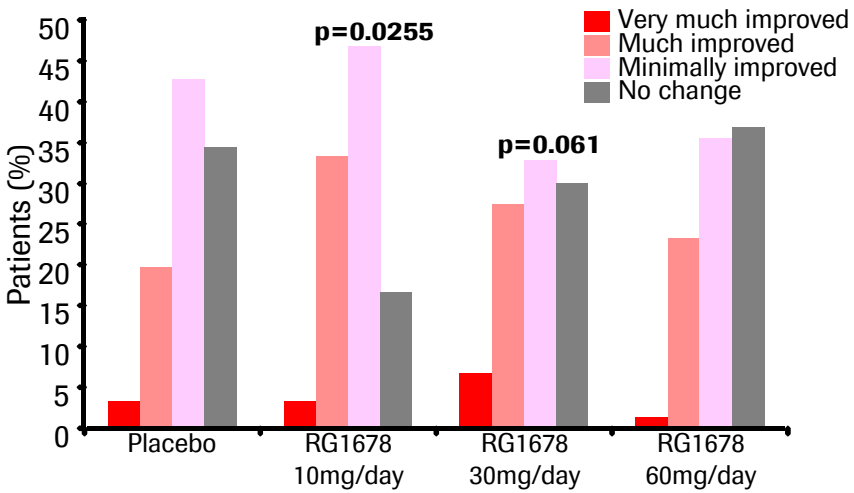
*PP population

Consistent effects on all measured outcomes*

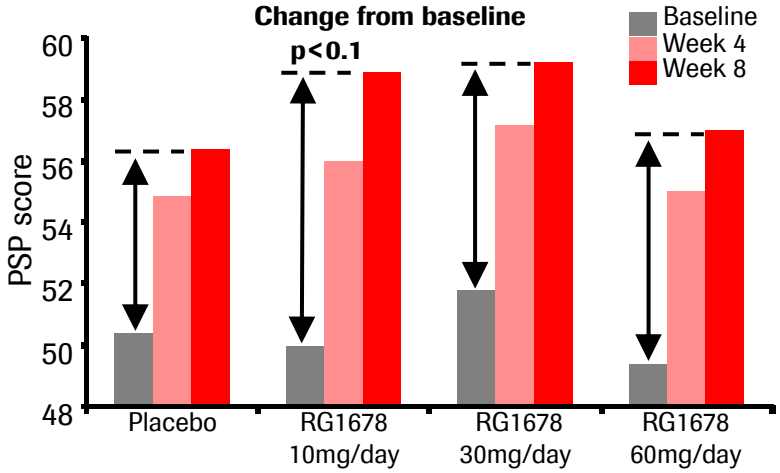
Response rate



CGI-I of negative symptoms



Change in function (PSP)



*PP population; Response rate: ≥20% improvement in NSFS; PSP=Personal and Social Performance; CGI-I=Clinical Global Impression-Improvement

GlyT-1 in phase III: exploring two indications

Negative symptoms and sub-optimally controlled patients

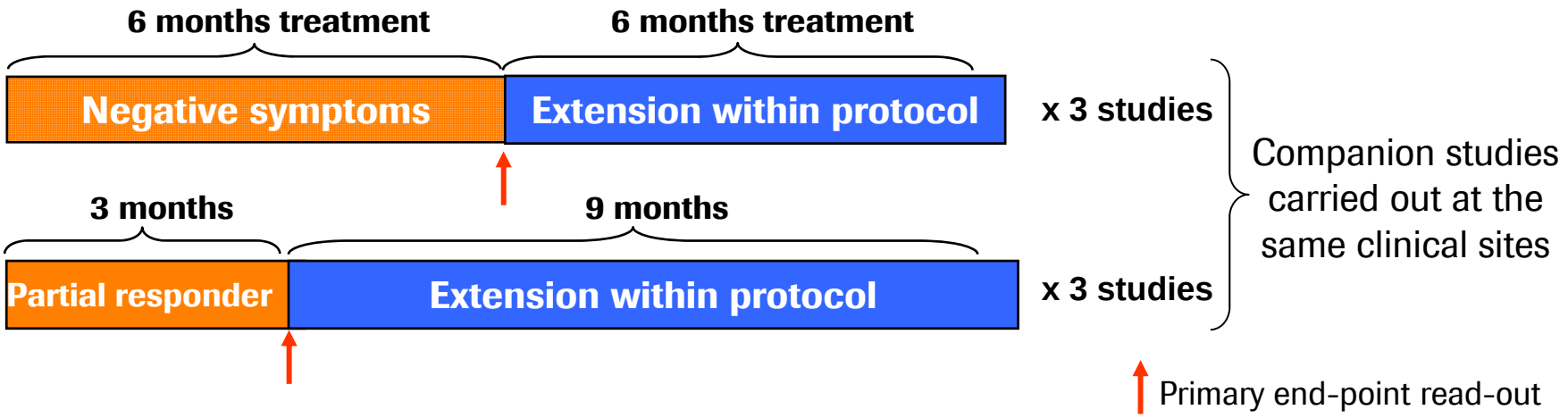
	Negative symptoms of schizophrenia (3 trials)	
	2x	**1x**
No. of patients	N=620 1:1:1 randomisation	N=620 1:1:1 randomisation
Primary endpoint	PANSS negative symptoms factor score at week 24	
Design	**ARM A:** 10 mg GlyT-1 **ARM B:** 20 mg GlyT-1 **ARM C:** placebo	**ARM A:** 5 mg GlyT-1 **ARM B:** 10 mg GlyT-1 **ARM C:** placebo
Status	FPI Q4 2010; Expect data 2013	

Patients with sub-optimally controlled symptoms of schizophrenia (3 trials)	
2x	**1x**
N=600 1:1:1 randomisation	N=600 1:1:1 randomisation
PANSS positive symptoms factor score at week 12	
ARM A: 10 mg GlyT-1 **ARM B:** 20 mg GlyT-1 **ARM C:** placebo	**ARM A:** 5 mg GlyT-1 **ARM B:** 10 mg GlyT-1 **ARM C:** placebo
FPI Q4 2010; Expect data 2013	

Two new indications, study designs and patient populations agreed with health authorities in US (SPA), Europe and Japan

GlyT-1 development: optimizing the data quality

Synergies in study design and patient recruitment

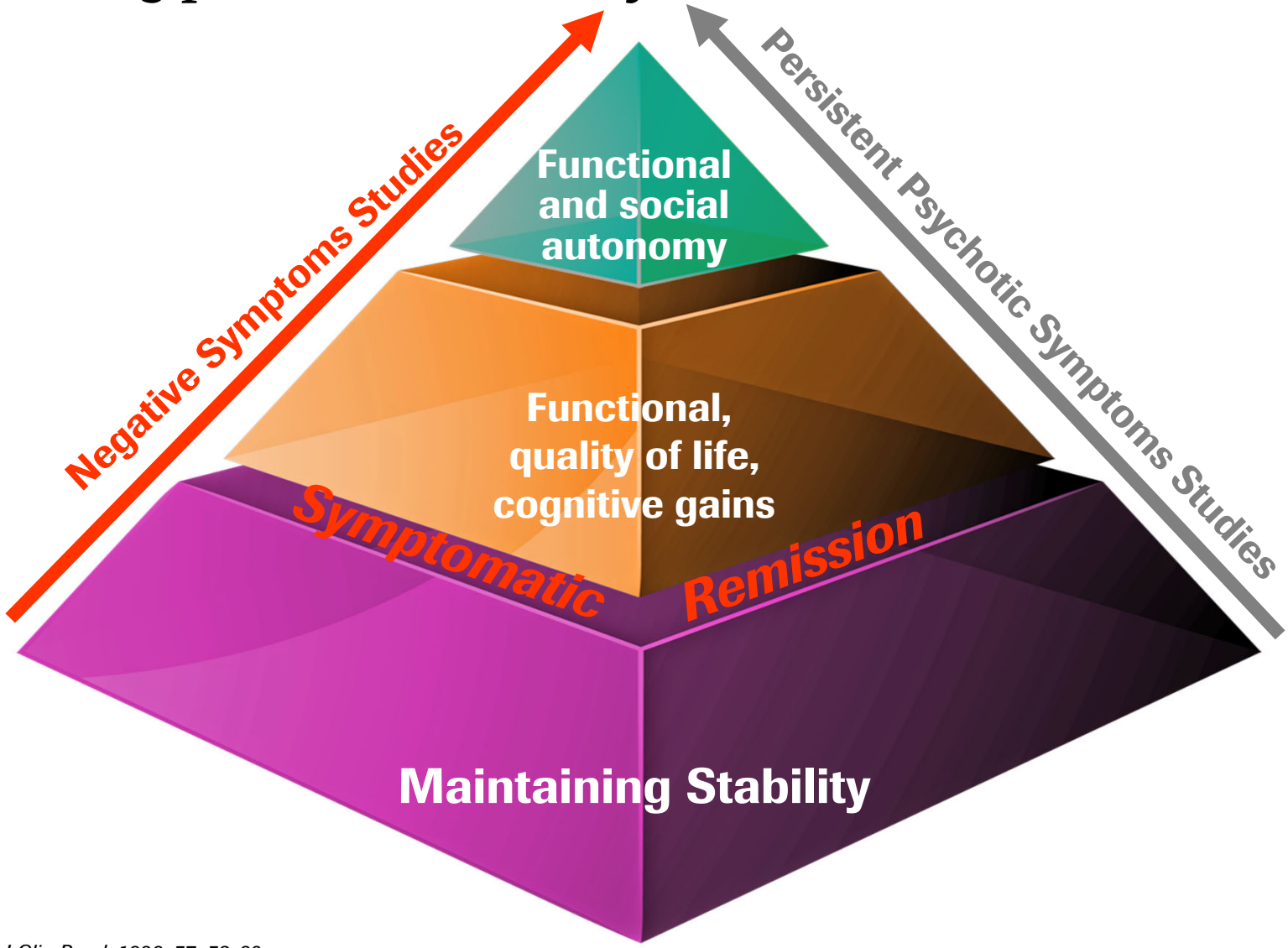


Studies for negative symptoms and partial responders developed in parallel at the same clinical sites:

- High unmet medical need in both indications
- Creates broad safety data base
- Synergy in recruitment: reduced risk of rater inflation/deflation

Treatment goal in schizophrenia

Restoring patient autonomy

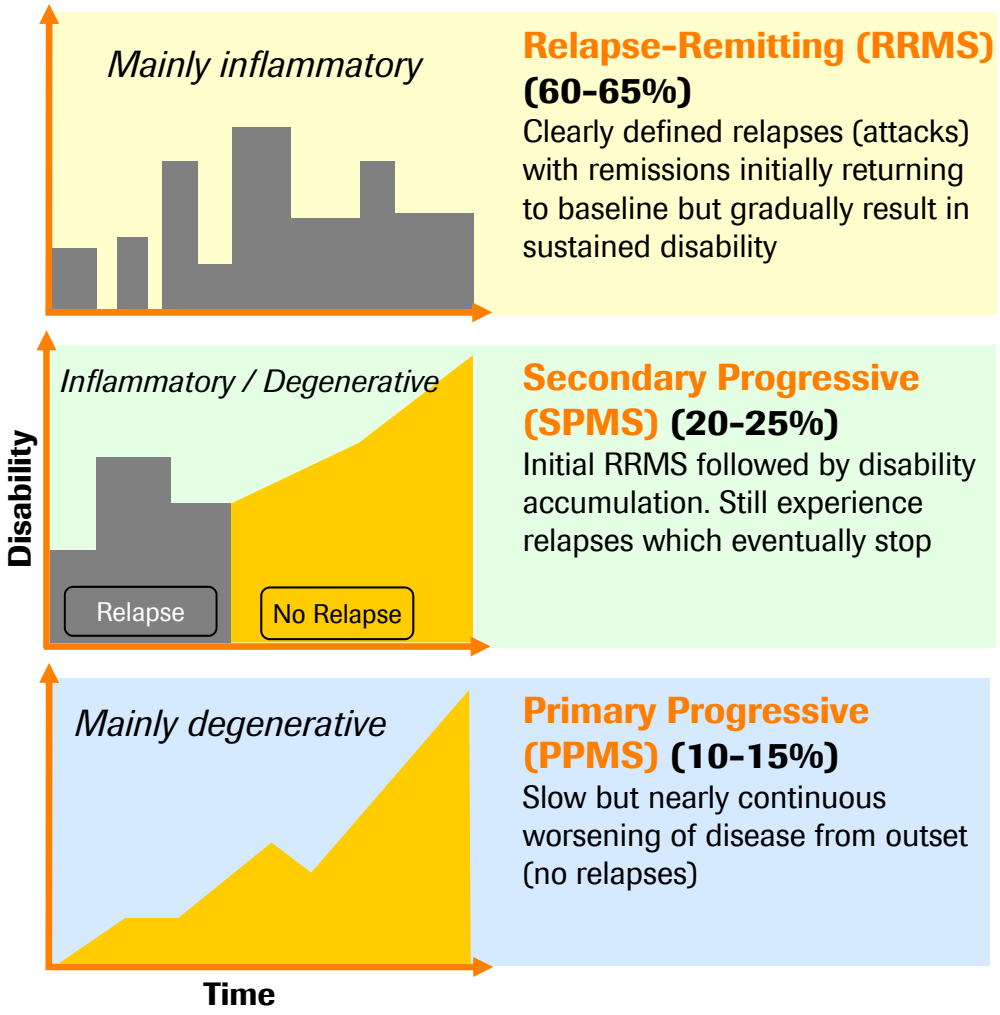


* Weiden et al, *J Clin Psych* 1996; 57: 53-60

Ocrelizumab

Humanized anti-CD20 antibody

Three major types of Multiple Sclerosis



Adapted from Lublin 1996, Arnold 2004

Marketplace

- High unmet need:
  - high efficacy therapies for relapsing forms have major safety issues
  - no treatment for primary progressive disease
  - diagnosis and classification is difficult, often retrospective and can take 2-5 years
- Treatment decisions concentrated mainly in MS centers/hospitals
- Payers pressure has been limited; patients' advocacy groups powerful in access

Current treatment dominated by ABCR cycling

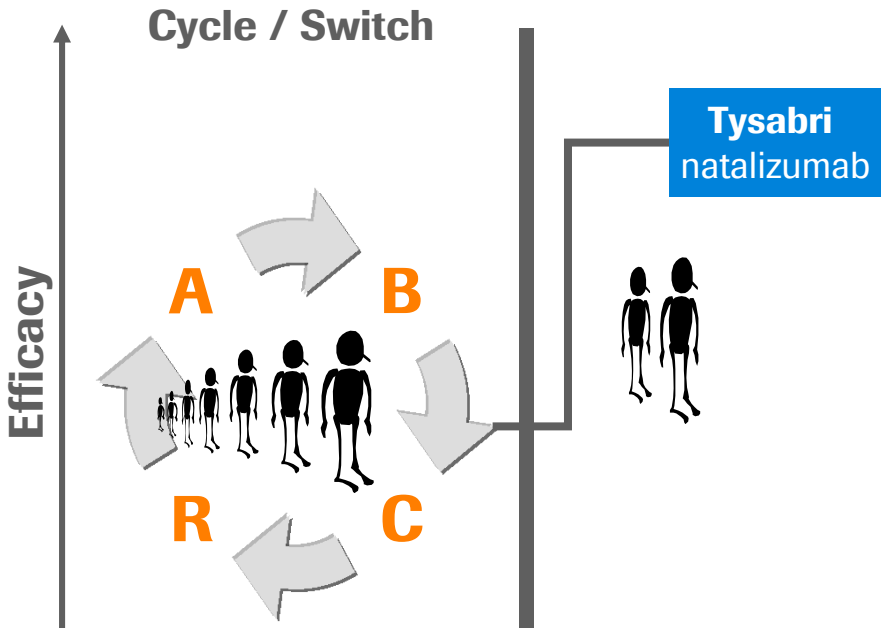
"Between a rock and a hard place"

Available treatment options

Avonex interferon ß1a	**B**etaferon interferon ß1b
Copaxone glatiramer acetate	**R**ebif interferon ß1a
Gilenya fingolimod	**Tysabri** natalizumab

Treatment choice:

- Efficacy/safety trade-off
- Potential risks:
  - ABCR: Injection site reactions
  - Tysabri: opport. infect.: PML, liver toxicity
  - Gilenya: cardiovascular- , respiratory effects, livertoxicity, macular edema, lymphomas, fetal risk



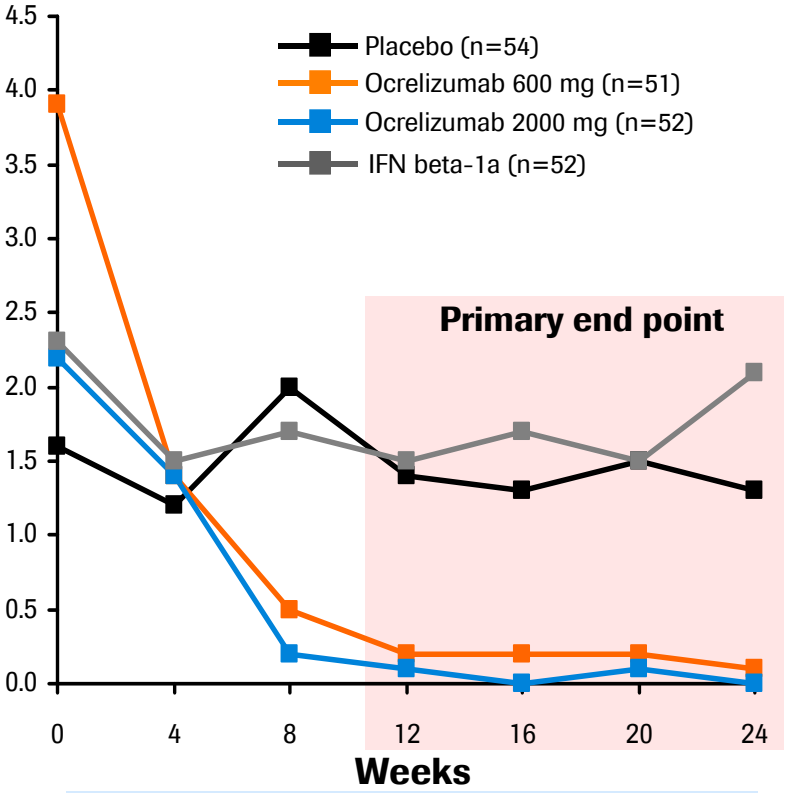
Initial management
Switches due to flu, injection site reactions or injection frequency

Failure-switch
based on ABCR efficacy or tolerability issues

Ocrelizumab in phase II

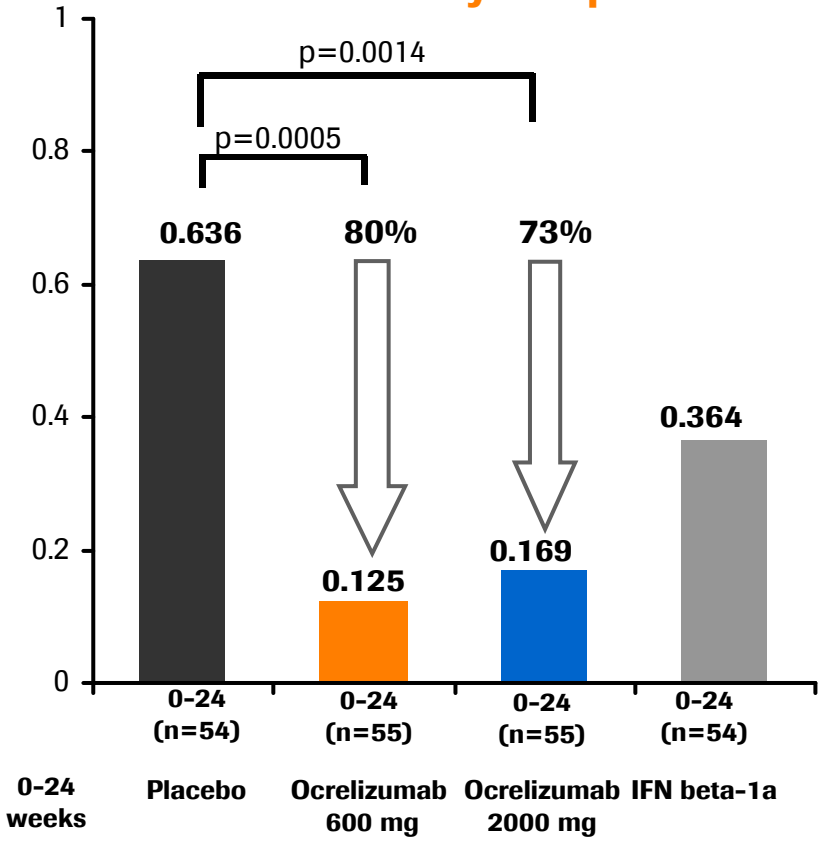
Efficacy amongst the highest seen in RRMS

Mean no. T1 Gd-enhancing lesions



Reductions of 96 % (2000mg) and 89 % (600mg); p<0.0001 for both ocrelizumab doses vs placebo

Annualized Relapse Rate (ARR) Secondary end point

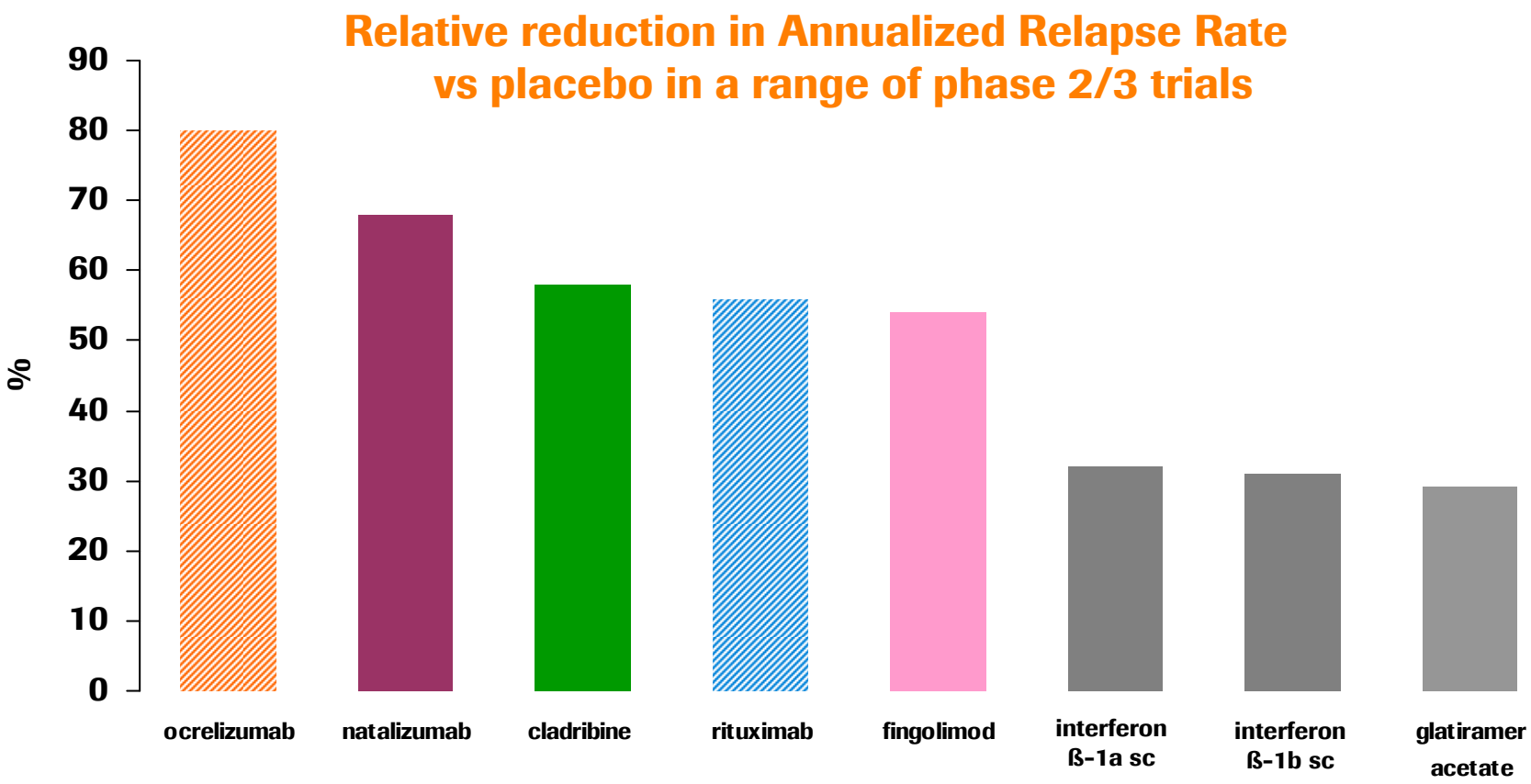


Gd=Gadolinium; IFN beta-1a arm was open label, all efficacy comparisons were exploratory

Kappos et al, ECTRIMS 2010

Ocrelizumab in RRMS

Looking for the next step in MS therapy



NOTES:

- Pattern: *Solid bars represent Phase III studies; pattern = Phase II*
- *Trial durations vary from 6 mos. to 3 yrs; studies included different patient populations, different in/exclusion criteria, different ARR definitions and data were collected over a time span of more than 20 years*
- Ph II trials of laquinimod, teriflunomide, and BG12 did not show significantly better efficacy on ARR than placebo and are not included in comparison figures

Ocrelizumab Phase III program in RMS and PMMS

Patient population	Relapsing multiple sclerosis (RMS)		Primary progressive multiple sclerosis (PPMS)
Phase/study	**Phase III OPERA I**	**Phase III OPERA II**	**Phase III ORATORIO**
# of patients	N=800	N=800	N=630
Design	• 96-week treatment period: ▪ **ARM A:** Ocrelizumab 2x 300 mg IV every 24 weeks ▪ **ARM B:** Rebif® (interferon β-1a)	• 96-week treatment period: ▪ **ARM A:** Ocrelizumab 2x 300 mg IV every 24 weeks ▪ **ARM B:** Rebif® (interferon β-1a)	• 120-week treatment period: ▪ **ARM A:** Ocrelizumab 2x 300 mg IV every 24 weeks ▪ **ARM B:** Placebo
Primary endpoint	▪ Annualized relapse rate at 96 weeks versus Rebif	▪ Annualized relapse rate at 96 weeks versus Rebif	▪ Sustained disability progression versus placebo by Expanded Disability Status Scale (EDSS)
Status	▪ Expect FPI Q3 2011	▪ Expect FPI Q3 2011	▪ FPI Q1 2011

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