



german  
science day

02. Februar 2012  
Berlin

## **Fight Cancer! Eine Initiative der Deutschen Biotechnologie**

### **Optimizing Antibodies to Fight Cancer: MOR208 as a New Approach in B-cell Malignancies**

**Dr. Arndt Schottelius**  
**Chief Development Officer**

**morphosys**  
Engineering the Medicines of Tomorrow



## **Broad Pipeline**

78 drug programs – 20 in clinical trials  
~35% programs in cancer



## **Proven Source for Therapeutic Antibodies**

Industry's most successful antibody library HuCAL



## **Growing Footprint in Diagnostics**

Novel diagnostic products in cancer and other



## **Financial Strength**

Profitable, strong balance sheet



## **Experienced Management Team**

More than 80 years of pharma & biotech experience



# Why Antibodies?

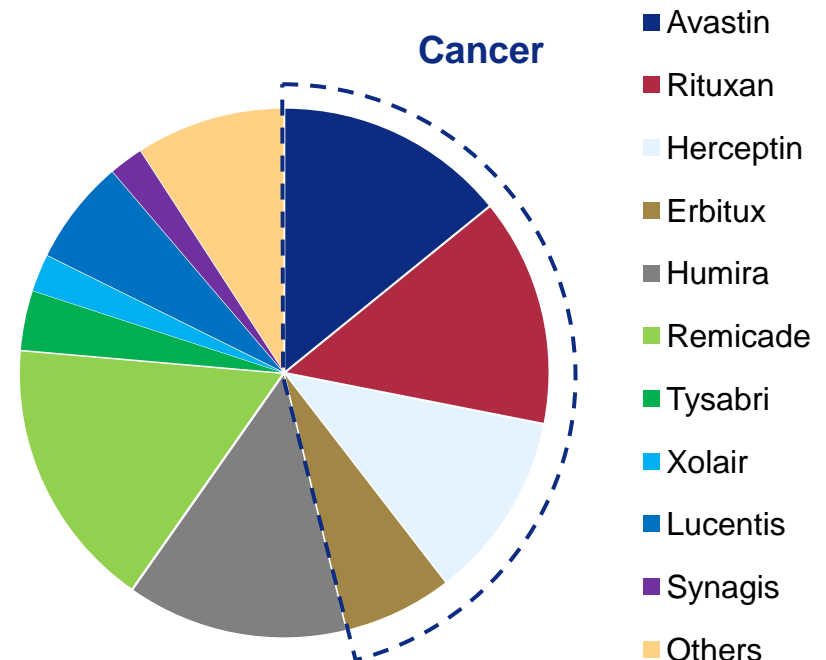
- Most successful biological drugs
- Long half-life, dosing advantage
- No off-target toxicity
- Various formats available, can be combined with toxins, etc.
- Many indications addressable
- Complexity limits entry of generics

## The MorphoSys Edge

- In-built optimization allows us to “dial-in” drug properties
- Fully human

→ Fastest growing class of therapeutics in the pharmaceutical industry

## Antibody Product Sales 2010

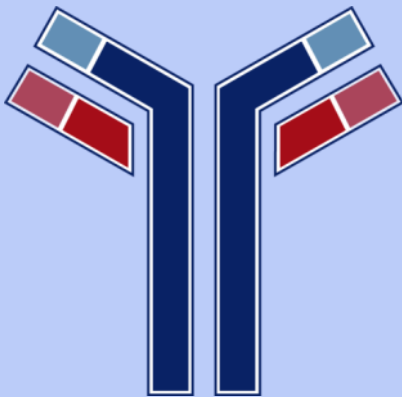


**Total Sales 2010: \$ 48bn**

# Approaches to „Beef up“ Today’s Antibody Therapies

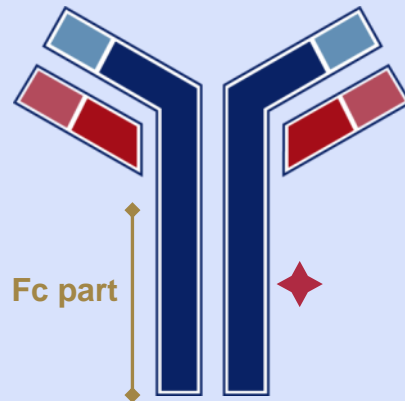
## “Naked” Antibodies

Closest to Nature  
Easiest to Produce



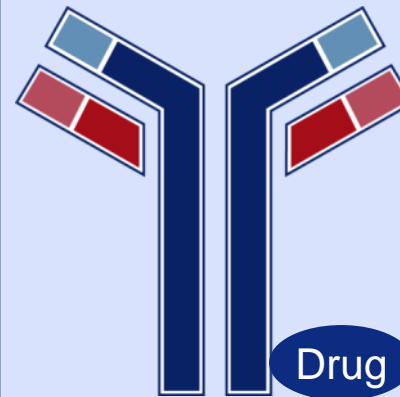
## Antibodies with optimized “Fc” part

Higher Cell Killing  
Production still easy



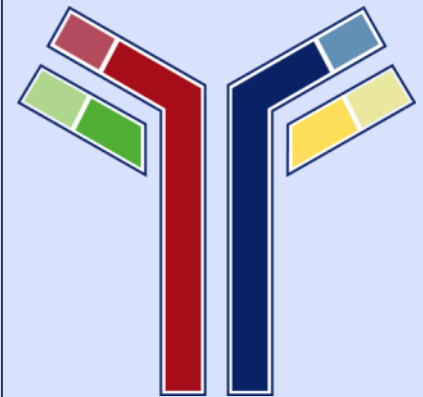
## “Armed” Antibodies

Delivery of Toxin  
Difficult to Produce



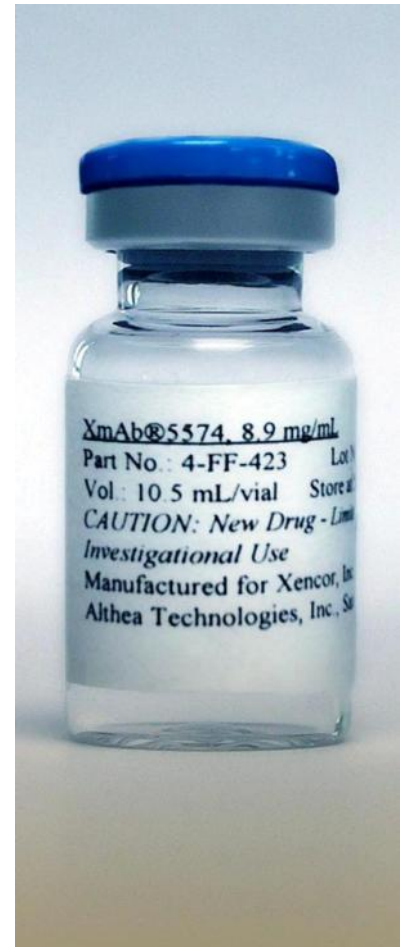
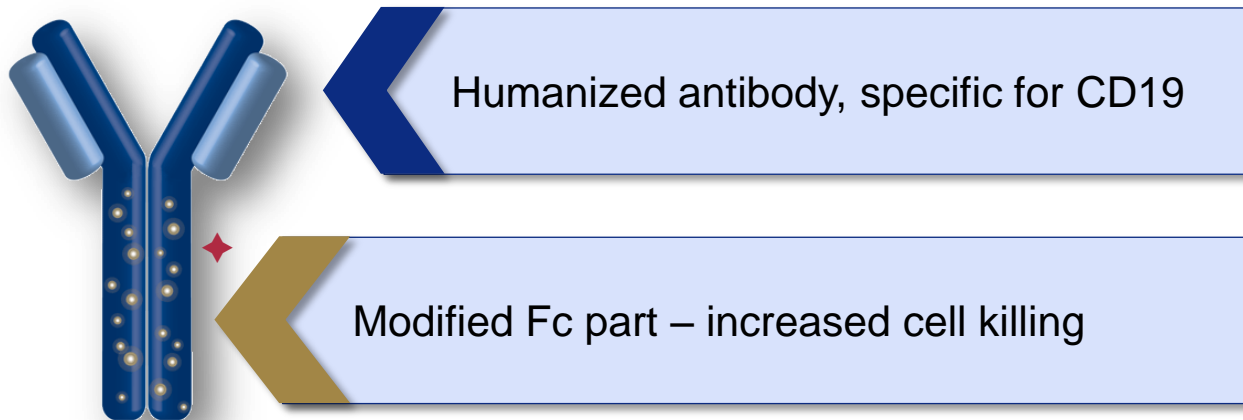
## Bi-/Tri-functional Antibodies

Innovative Concept  
Difficult to Produce



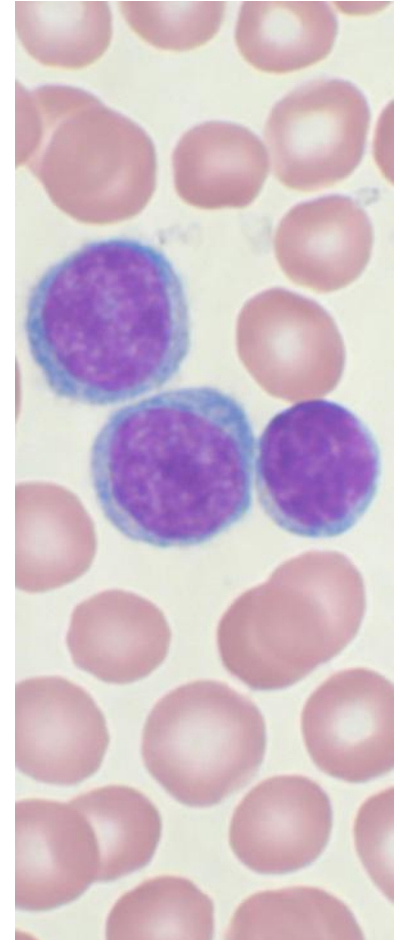
# MOR208 (XmAb<sup>®</sup>5574) as a New Approach in B-cell Malignancies

- Humanized antibody against CD19
- In-licensed from Xencor Inc. in 2010
- Comprises proprietary modification of the Fc part of the antibody leading to rapid and sustained target cell depletion
- Phase 1 trial for CLL ongoing in the US



# Some Facts About B Cell Malignancies

- B cell malignancies are also known as leukemias & lymphomas, e.g. chronic lymphoid leukemia (CLL), acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma (NHL)
- Approximately 77,000 new cases of NHL, CLL (8,000) and B-precursor ALL (3,000) diagnosed in the U.S. per year
- High unmet medical need as many patients relapse
- Trend towards combination therapies and new mode of actions
  
- Current targeted treatment option: Rituxan<sup>®</sup> (rituximab) and various combination therapies
  - CD20 antibody
  - Blockbuster drug with annual sales in excess of US\$ 6.6 million (2010)



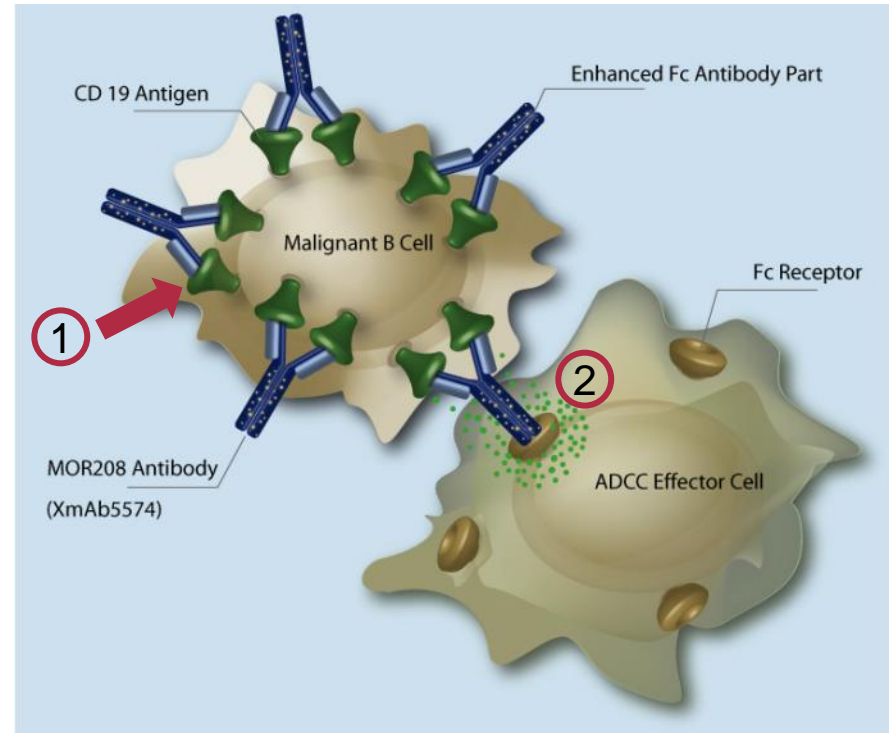
# Anti-tumor Mechanisms are Mediated by IgG – Fc Receptor Interactions

Two interactions are key for mAb activity:

- ① mAb binding to the tumor-associated antigen (here CD19)
- ② Binding of Fc receptor on effector cell (e.g. NK cell ) to the Fc portion of the mAb and recruitment of effector cell to kill tumor cell

## Rationale for Fc optimization:

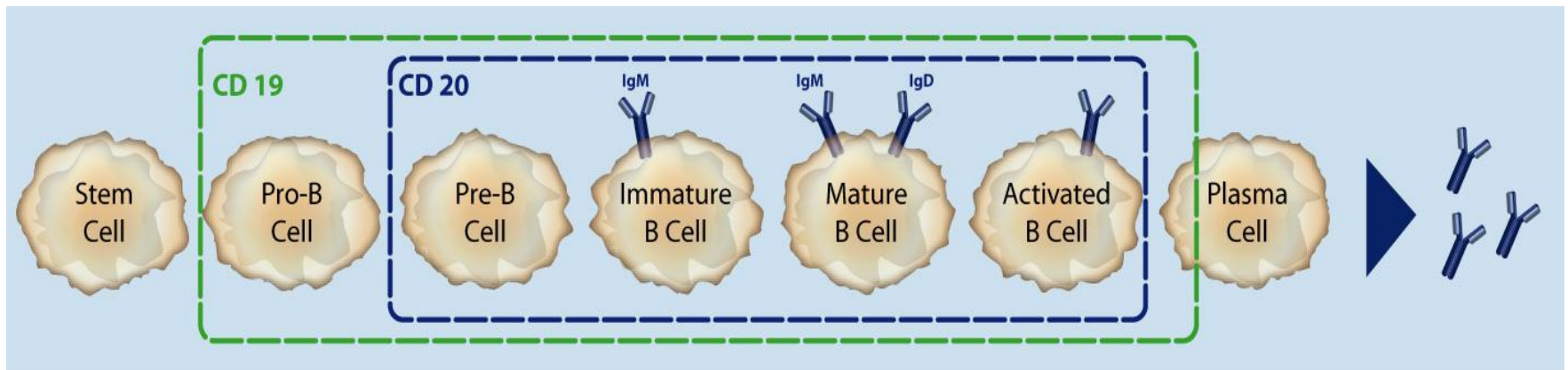
- Enhanced ADCC (antibody dependent cellular cytotoxicity) response
- Enhanced phagocytosis by macrophages



MOR208: Fc Optimization for Increased Tumor Killing

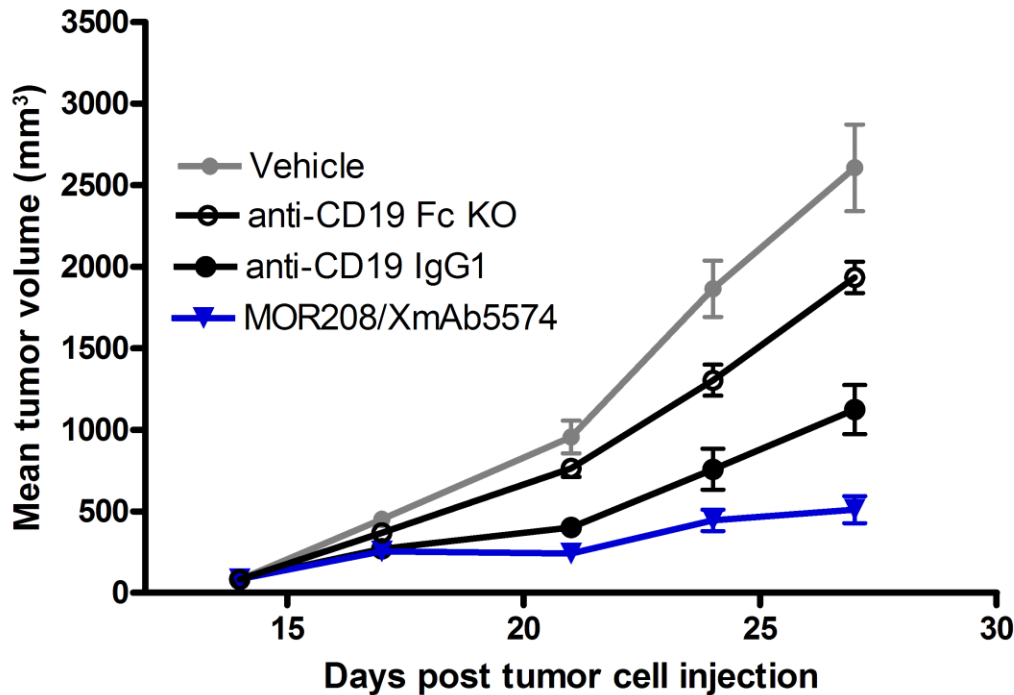
# Anti-CD19 Antibodies Hold Promise for the Treatment of B-cell Malignancies

- Broader expression of CD19 in B-cell tumors compared to CD20
- Potential for use in patients with Rituxan® (rituximab) resistance
- Encouraging clinical data with CD19 bispecific antibody in NHL and ALL validates CD19 as a new target



Success of B-cell depletion in lymphoma opens many possibilities for novel regimens

# Efficacy Against Established Tumors is Fc $\gamma$ R-Dependent and Enhanced by Fc Engineering

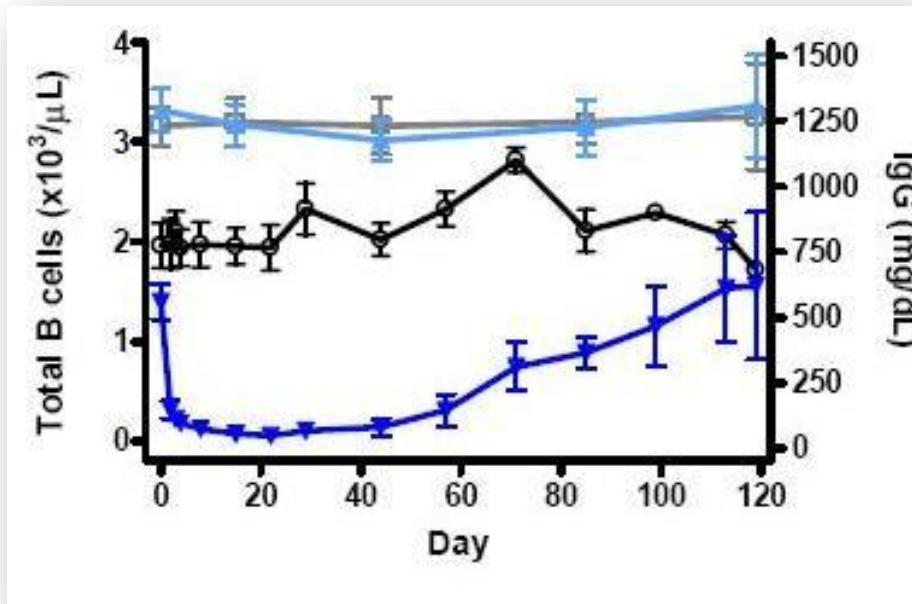


- Human tumor xenograft in SCID mice
- 40-120 mm<sup>3</sup> Ramos tumors at start of Ab treatment
- 10 mg/kg Ab, 2x/week for 3 weeks, 10 mice/group

anti-CD19 Fc KO: full length anti-CD19 with two mutations that remove Fc $\gamma$ R binding  
anti-CD19 IgG1: unmodified IgG1

Horton HM et al. *Cancer Res* 2008;68:8049-57

# MOR208/XmAb5574 Showed Rapid and Sustained Depletion of B cells in Cynomolgus Monkeys

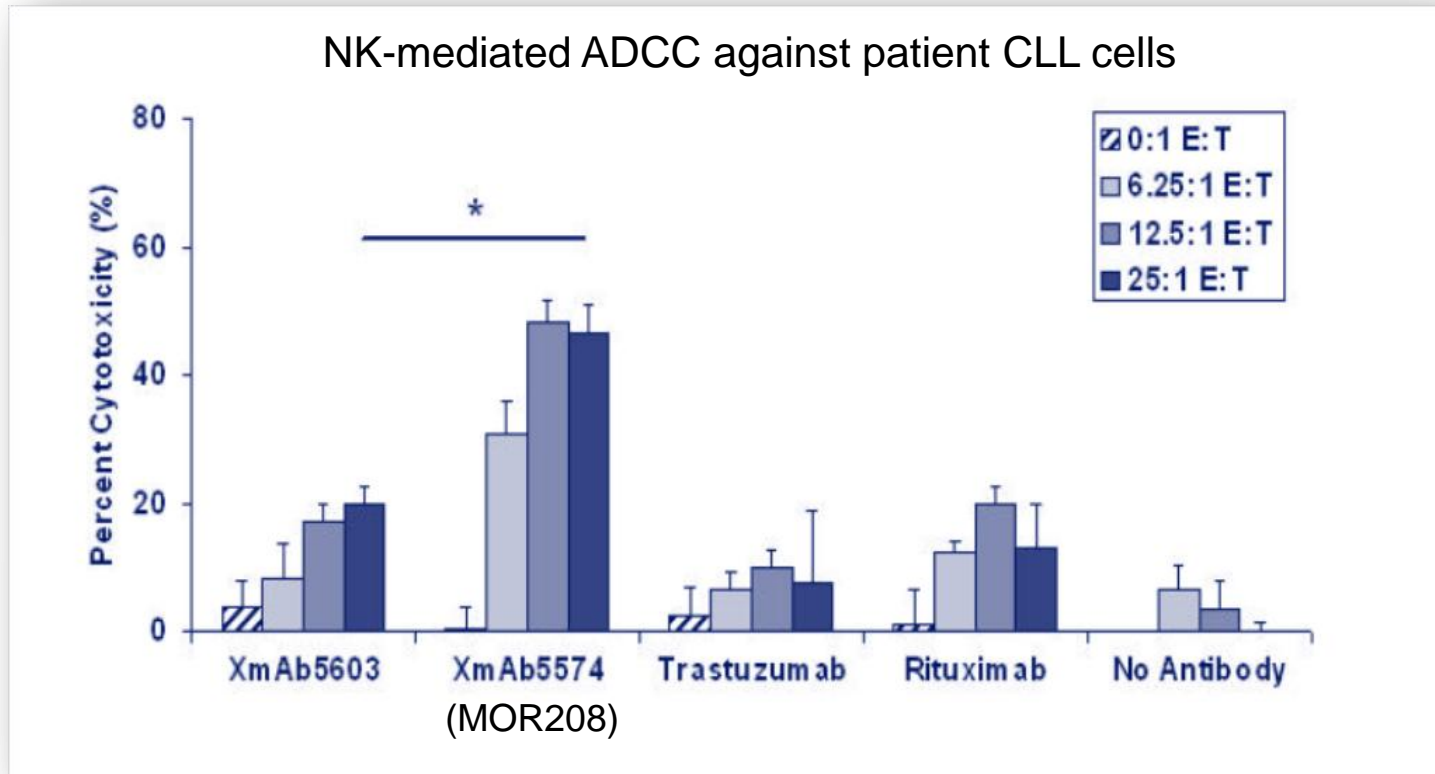


- Single IV dose, 10 mg/kg (1 hr)
- N = 6 monkeys /group
- 2 groups, vehicle, MOR208/XmAb5574

▼ MOR208/XmAb5574 – B cells      ○ Vehicle – B cells  
 ▲ MOR208/XmAb5574 – Serum IgG      □ Vehicle – Serum IgG

Source: Xencor Inc.

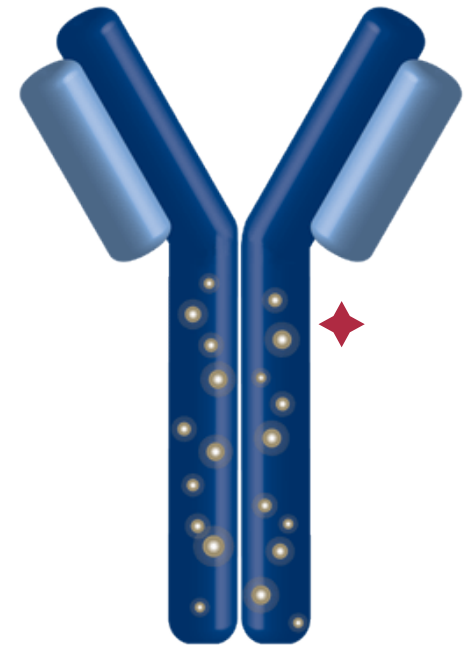
# MOR208/XmAb5574 Induces Potent ADCC Against Patient-Derived B-CLL Cells



*Awan et al., Blood 2010*

# MOR208 is Competitive in the CD19 Antibody Space

- Expected half life favoring convenient dosing schedule
- i.v. administration
- Straightforward manufacturing
- Potential for good safety profile
- Embraces a number of effector mechanisms
  - Significantly increased ADCC compared to Rituxan *in vitro*
  - Enhanced Fc $\gamma$ R1a affinity may enhance macrophage function, and result in improved tissue B-cell depletion



Fc domain modification of MOR208 embraces a broader range of effector mechanisms

## Design

- Multicentre, open-label, multi-dose, single-arm phase 1, dose-escalation study (USA)

## Population

- Patients with CLL/SLL, who have not responded to or have become refractory to previous therapies

## Objectives

- Investigate maximum tolerated dose, safety and tolerability
- Pharmacokinetics and immunogenicity
- Assess preliminary anti-tumor activity

## Clinical Data

- Data will become available in 2012

## Next Steps

- MorphoSys plans to initiate additional trials in other B cell malignancies



# MorphoSys's Antibody Pipeline – One of the Broadest in the Industry



Program	Partner	Indication	Discovery	Pre-clinic	Phase 1	Phase 2
MOR103 (2 programs)	-	Rheumatoid arthritis, Multiple sclerosis				
not discl.	Novartis	not discl.				
CNTO888 (2 programs)	Centocor/J&J	<b>Cancer</b> Idiopathic pulmonary fibrosis				
Gantenerumab	Roche	Alzheimer's Disease				
BHQ880	Novartis	<b>Cancer</b>				
BYM338	Novartis	Musculoskeletal				
CNTO 1959	Centocor/J&J	Psoriasis				
MOR208	-	<b>Cancer</b>				
MOR202	-	<b>Cancer</b>				
CNTO 3157	Centocor/J&J	Asthma				
not discl.	Centocor/J&J	Inflammation				
not discl.	Novartis	Ophthalmology				
not discl.	Novartis	Inflammation				
not discl.	Boehringer Ingelheim	not discl.				
not discl.	Pfizer	<b>Cancer</b>				
OMP-59R5	Oncomed	<b>Cancer</b>				
OMP-18R5	Oncomed	<b>Cancer</b>				
BAY94-9343 (ADC)	Bayer HealthCare	<b>Cancer</b>				
25 Partnered Programs	Various Partners	Various Indications				
33 Programs, incl. 2 co-dev with Novartis	Various Partners	Various Indications				

**68 Partnered Programs**  
**10 Proprietary Programs**

# Thank You



[www.morphosys.com](http://www.morphosys.com)

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