

# Better Antibodies By Design

Goldman Sachs Biotech Symposium, London, UK September 5, 2014



## Forward Looking Statement

This presentation contains forward looking statements. The words "believe", "expect", "anticipate", "intend" and "plan" and similar expressions identify forward looking statements. All statements other than statements of historical facts included in this presentation, including, without limitation, those regarding our financial position, business strategy, plans and objectives of management for future operations (including development plans and objectives relating to our products), are forward looking statements. Such forward looking statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding our present and future business strategies and the environment in which we will operate in the future. The important factors that could cause our actual results, performance or achievements to differ materially from those in the forward looking statements include, among others, risks associated with product discovery and development, uncertainties related to the outcome of clinical trials, slower than expected rates of patient recruitment, unforeseen safety issues resulting from the administration of our products in patients, uncertainties related to product manufacturing, the lack of market acceptance of our products, our inability to manage growth, the competitive environment in relation to our business area and markets, our inability to attract and retain suitably qualified personnel, the unenforceability or lack of protection of our patents and proprietary rights, our relationships with affiliated entities, changes and developments in technology which may render our products obsolete, and other factors. Further, certain forward looking statements are based upon assumptions of future events which may not prove to be accurate. The forward looking statements in this document speak only as at the date of this presentation.



## **Antibody Innovation Generating World Class Products**



#### Focus on Cancer

- Differentiated human antibodies
- Track record breakthrough therapeutics



#### Robust Product Pipeline

- Ofatumumab cancer & autoimmune potential (marketed as Arzerra® in various CLL indications)
- Daratumumab blockbuster potential
- HuMax®-TF-ADC in Phase I solid cancers



#### Passion for Innovation

- World class antibody know-how
- Proprietary technologies DuoBody<sup>®</sup> & HexaBody<sup>™</sup>
- Innovative pre-clinical pipeline



#### Partnerships → Product Ownership

- Key collaborations drive current pipeline
- Product opt-ins + retain products for future value
- Well capitalized



# **Innovative Pipeline**

		Development Phase			
Product	Disease Indications	Pre- I I/II II III			
Ofatumumab 18 studies	Chronic lymphocytic leukemia (CLL)				
Target: CD20	Follicular lymphoma (FL)				
Partner: GSK	Waldenström's macroglobulinemia (WM)				
	Pemphigus vulgaris (PV)				
	Relapsing remitting multiple sclerosis (RRMS)	Ammounteed			
	Neuromyelitis optica (NMO)	Announces			
Daratumumab 8 studies Target: CD38 Partner: Janssen	Multiple myeloma (MM)				
HuMax-TF-ADC Target: TF Partner: Seattle Genetics	Solid Cancers				
<b>Teprotumumab</b> 2 studies Target: IGF-1R Partner: River Vision	Active thyroid eye disease				
	Diabetic macular edema				
> 10 Active	Partnered programs: HuMab, DuoBody & HexaBody				
Pre-clinical Programs	Proprietary programs: HuMab, HuMab-ADC, DuoBody, DuoBody-ADC & HexaBody				



# Daratumumab (HuMax®-CD38) First-in-Class Antibody with Broad-Spectrum Killing Activity

# Additional Potential Blood Cancer Indications

 ALL, AML, DLBCL, FL, Plasma Cell Leukemia, Mantle Cell Leukemia, CLL

#### First-in-Class Fully Human Antibody

- Targets CD38 5 different ways of attacking cancer cells
- Multiple Myeloma & other blood cancers
- Blockbuster potential
- · Promising early clinical MM data
- Broad & expansive development in MM
- Breakthrough Therapy Designation

#### Partner: Janssen Biotech

- Janssen funds development & commercialization
- > \$1.1B potential deal value, + double-digit royalties
- Zero cost / limited financial risk for Genmab



# Expansive Daratumumab Development 9 Ongoing or Announced Studies in Multiple Myeloma

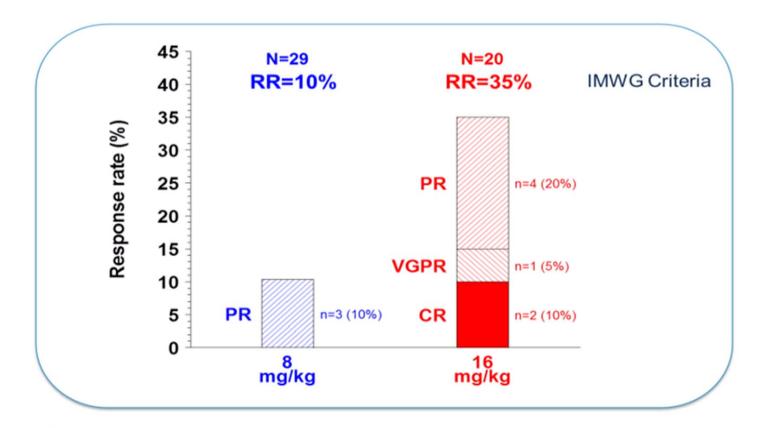
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	Disease Stage	Therapy	Development Phase			
Indication			Pre- I I/II II III IV clinical			
Multiple Myeloma	Front line (transplant & non- transplant)	Dara + VMP*				
		Dara + Revlimid + Dex*				
		Multi combo 1 Study				
	Relapsed or Refractory	Dara + Revlimid + Dex 2 Studies				
		Dara + Velcade + Dex 1 Study				
		Mono, Japan				
		Mono, safety				
	Double Refractory	Mono, BTD population				
	Smoldering		In planning			
	Maintenance		Integrated into some study protocols			
Non-MM	Various	Potential in: ALL, AML, DLBCL, FL, Plasma Cell Leukemia, Mantle Cell Leukemia, CLL				

<sup>\*</sup>Phase III studies announced but not yet started.



## Daratumumab: Early Signs of Clinical Activity Phase I/II Monotherapy Study

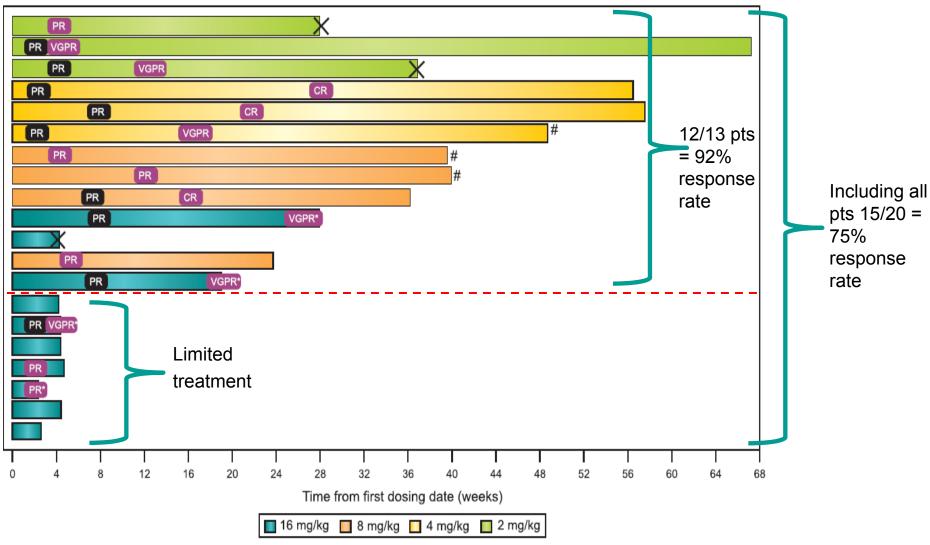
- Relapsed and refractory multiple myeloma, ASCO 2014
- Safety & efficacy in 49 patients
- 35% response rate at 16 mg/kg
- Treatment well tolerated



Data presented at ASCO 2014



# Daratumumab: Early Signs of Clinical Activity Ph I/II Revlimid Combo Study in Multiple Myeloma





## Arzerra® (ofatumumab)

# Sales Growth by GSK

- 2013 sales GBP 74.9M (~\$124M); royalty DKK 131M
- Genmab Cancer Royalty = 20%



#### **Our First Marketed Product**

- Fully human antibody targeting CD20 on cancerous B-cells
- Differentiated vs other CD20 mAb, targets slice of > \$7B market

#### Cancer

- Approved\*
  - US 1st Line CLL in combo w/ chlorambucil
  - EU 1<sup>st</sup> Line CLL in combo w/ chlorambucil or bendamustine
  - Fludarabine and alemtuzumab refractory CLL
- 7\*\* Phase III trials in CLL & FL
- Novartis potential partner 2015 (subject to GSK / Novartis deal close)

#### **Autoimmune diseases (unapproved)**

- Phase III trial ongoing in PV
- Relapsing remitting MS Ph IIIs & pivotal NMO trial announced
- Partnered with GSK

<sup>\*</sup>In US approved in combination with chlorambucil for the treatment of previously untreated patients with CLL for whom fludarabine-based therapy is considered inappropriate as well as for the treatment of patients with CLL refractory to fludarabine and alemtuzumab.

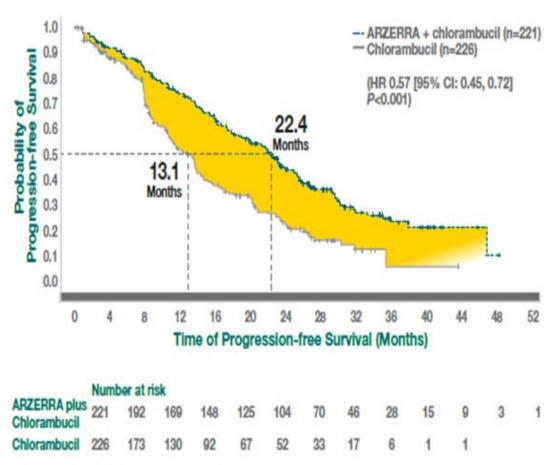
In EU approved in combination with chlorambucil or bendamustine for the treatment of patients with CLL who have not received prior therapy and who are not eligible for fludarabine-based therapy, as well as for the treatment of patients with CLL refractory to fludarabine and alemtuzumab.

<sup>\*\*</sup>Source: clinicaltrials.gov



# Arzerra Label Expansion: Phase III Data Ofatumumab + Chlorambucil Extends Progression Free Survival

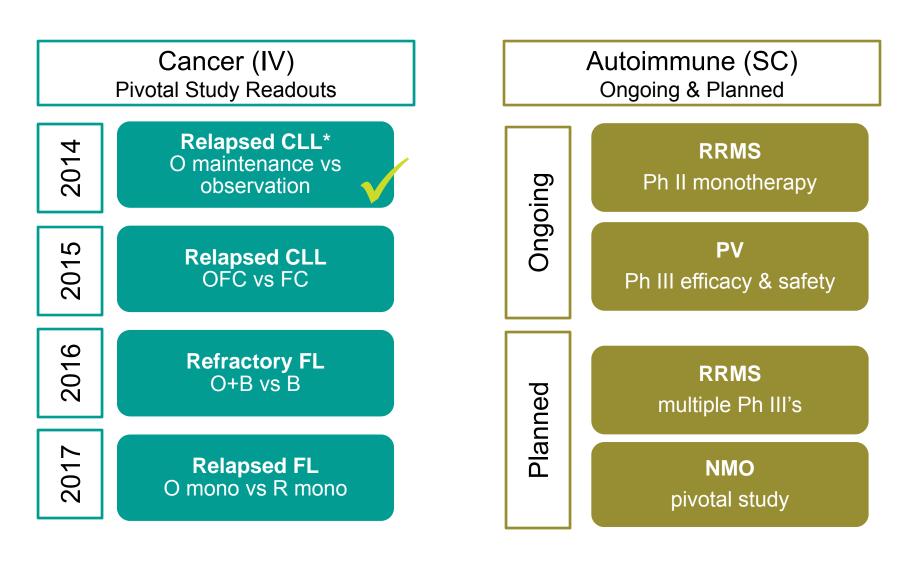
- Ofa + chlorambucil vs chlorambucil in front line CLL
- 71% improvement in PFS
- No unexpected safety findings - Most common SAFs:
  - Neutropenia (5%), anemia (4%), pneumonia (4%) and pyrexia (2%)







## Ofatumumab: Planned & Ongoing Trials

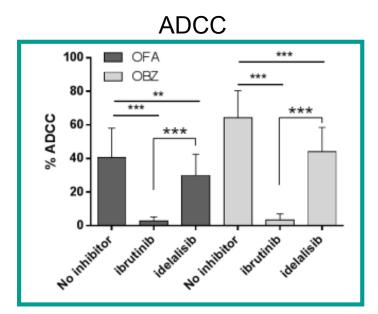


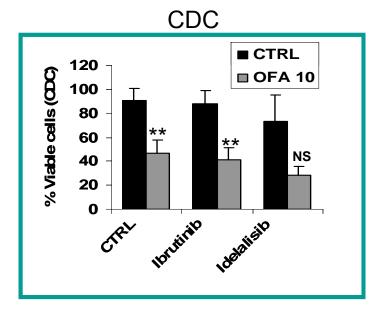
Note: The indications above are unapproved \*Interim data reported



#### Ofatumumab:

## Potential to Combine with Tyrosine Kinase Inhibitors





TKIs knock out immune effector cells (NK cells, macrophages) so ADCC ineffective

Ofatumumab most active CDC killing compared to other CD20 mAb Ibrutinib ofatumumab combination highly active in CLL, ISS study at ASCO 2014

#### Sources:

Da Roit et al. "Ibrutinib interferes with the cell-mediated anti-tumor activities of therapeutic CD20 antibodies: implications for combination therapy." Abstract. EHA 2014

Jaglowski et al. "A Phase Ib/II study evaluating activity and tolerability of the BTK inhibitor ibrutinib in combination with ofatumumab in patients with chronic lymphocytic leukemia / small lymphocytic lymphoma (CLL/SLL) and related diseases." ASCO 2014

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#### Ofatumumab - Future in Autoimmune

#### Multiple Ph III Trials to Start in Autoimmune Indications

#### Relapsing Remitting Multiple Sclerosis (RRMS)

- Phase III's in RRMS expected to begin in 2015
  - Follow encouraging Phase II data
    - Sustained reduction cumulative number new brain lesions over 12 week period
    - No unexpected safety findings
- MS market forecast to peak at \$18.5B in 2018\*

#### **Neuromyelitis Optica (NMO)**

- GSK plans IND for potential pivotal study in NMO in 2014
  - NMO, a rare autoimmune disorder
  - No licensed therapy for NMO
  - Orphan indication

#### Pemphigus Vulgaris (PV)

- Phase III study ongoing
- Orphan indication



# HuMax®-TF-ADC: In the Clinic Next Generation Therapeutics

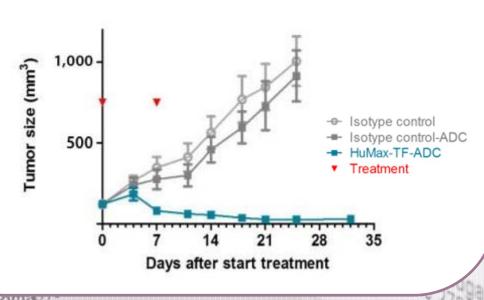
#### 8 Tumors

- Ovary, cervix, endometrium, bladder, prostate, head & neck, esophagus, lung
- Potential also in pancreatic cancer

#### Fully Human Antibody-drug Conjugate

- Targets Tissue Factor (TF)
- Strong pre-clinical data in multiple solid cancers
- Ongoing Phase I study
- Collaboration: Seattle Genetics opt-in (after Ph I/II)

Pre-clinical Cervical Cancer Model



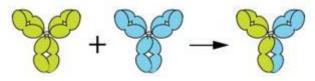


# DuoBody® Technology Efficient & Versatile Platform for Bispecific Antibodies



#### DuoBody

- Dual-targeting, potential to improve specificity & efficacy
- · Large scale manufacturing
  - Minimal protein engineering
  - Excellent quality BsAb at very high yields
- Differentiated from competitor platforms
  - Proper in vivo half-life
  - Fc-effector functions
- Good manufacturability



#### Ongoing Collaborations

- 2 Commercial deals
  - Novartis (2 programs, \$175M potential deal value + royalties)
  - Janssen Biotech (20 programs, \$3.6B potential deal value + royalties)
- 6 Research deals
  - Lilly, Kirin, Cormorant, undisclosed major Biotech, Agenus, BioNovion

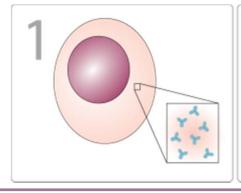


### HexaBody<sup>TM</sup> Technology Robust Effector Function Enhanced Antibodies

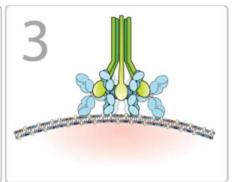


#### HexaBody

- Enables antibodies to more readily form clusters of 6 (hexamers)
- Induces & enhances target cell killing after binding via CDC
- CDC capability to essentially any antibody
- Builds on natural antibody biology minimal engineering
- Create novel, differentiated products in cancer & infectious disease
- Repurpose / rescue drug candidates that failed in Phase II/III
- Life cycle management
- First collaboration with undiscl. major Biotech, June 2014

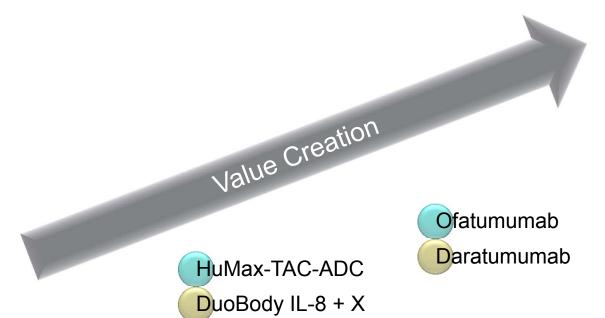








# **Creating Value With Our Technologies**



HuMax-TF-ADC
Pipeline products

Janssen DuoBody
Novartis DuoBody

Products / Technology
Validation

Exchange for technology

Many shots on goal

Greater value after PoC
Creates sustainable company



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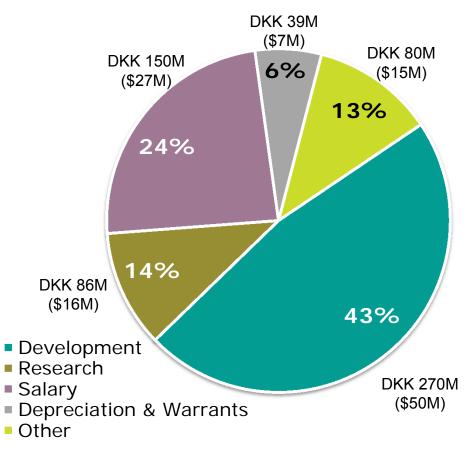
## Well-Capitalized Biotech – 2014 Guidance

Income Statement	DKKM	USDM*	
Revenue	800 - 875	147 - 160	
Operating expenses	(600) – (650)	(110) – (119)	
Operating income	175 – 250	32 - 46	

Cash Position	DKKM	USDM*
Cash position beginning of year**	1,557	285
Cash used in operations	0 – (50)	0 - (9)
Proceeds from private placement	972	178
Warrant exercises	33	6
Cash position at end of year**	2,450 – 2,550	449 - 467

<sup>\*</sup>USD 1.00 = DKK 5.4589

# 2014 Expense Base DKK 625M (\$115M)



2014 Guidance – August 13, 2014

<sup>\*\*</sup>Cash, cash equivalents and marketable securities



# 2014 Goals: Fueling Growth Through Our Platforms & Products

Priority	✓	Targeted Milestone
Maximize value of ofatumumab	2015 ✓ X X ✓	<ul> <li>» Ph III relapsed CLL ofa + FC data</li> <li>» Ph III maintenance CLL data</li> <li>» Ph III bulky refractory CLL ofa vs physician's choice data</li> <li>» Ph III relapsed DLBCL; ofa + chemo vs RTX + chemo data</li> <li>» Update progress sc autoimmune development</li> </ul>
Expansion Arzerra	<b>✓ ✓</b>	<ul><li>» CLL front line label expansion and launch</li><li>» Launch &amp; reimbursement in new countries</li></ul>
Fully exploit the potential of daratumumab	<ul><li>✓</li><li>✓</li></ul>	<ul> <li>» Ph I/II MM monotherapy matured efficacy data</li> <li>» Ph I/II MM dara + Revlimid safety &amp; efficacy data</li> <li>» Ph II MM monotherapy preliminary data</li> <li>» Ph Ib MM multi combo data</li> <li>» Start multiple new MM trials</li> <li>» Progress non-MM indications</li> </ul>
Expand pipeline		<ul><li>» Progress Ph I HuMax-TF-ADC study</li><li>» Report progress pre-clin. ADC, DuoBody &amp; HexaBody projects</li></ul>
Next generation technologies	✓ ✓ ✓	<ul> <li>» Enter new DuoBody technology collaborations</li> <li>» Report progress DuoBody collaborations</li> <li>» Start HexaBody technology collaborations</li> </ul>
Partnerships	✓	<ul><li>» Report progress partnered programs</li><li>» Enter new collaboration</li></ul>
Disciplined financial management	✓	<ul> <li>» Significant daratumumab milestones</li> <li>» No significant increase in cost base</li> <li>» Increase operating income and reduce cash burn</li> </ul>



# On Track to a Sustainably Profitable Future



- Robust differentiated product pipeline
  - Daratumumab, ofatumumab, HuMax-TF-ADC
  - Innovative pre-clinical pipeline
- Proprietary technologies -DuoBody & HexaBody
- Partnerships → Product ownership
  - Well capitalized
- Positioned for success
  - For patients & shareholders



# Better Antibodies By Design

**Appendix** 

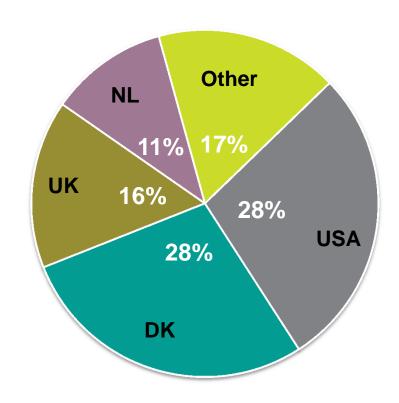




#### **International Shareholder Base**

- Major shareholders >5%
  - Johnson & Johnson Development Corporation
  - · Glaxo Group Ltd.
  - FMR (Fidelity)
  - ATP
- ADR program in USA
  - Ticker: GMXAY
  - Sponsored level 1
  - Ratio: 2 ADR: 1 ordinary share
  - Depositary Deutsche Bank
- Shares outstanding: 56,687,266
  - Total diluted shares: 62,054,820

# Geographical Shareholder Distribution January 31, 2014\*





# Market Sizes Estimated Prevalence in 7 Major Markets

Disease	Estimated Incidence in 7 Major Markets <sup>1</sup>	Estimated Prevalence	Estimated Global Branded Sales by 2018
CLL	32,000	250,000	\$5.3B
FL	32,000	260,000	\$10.5B <sup>2</sup>
MM	55,000	190,000	\$11.5B
RRMS	26,100³	370,600	\$18.5B³

Sources: CLL, DLBCL, FL 2013 forecast incidence: Datamonitor, "Pipeline Insight: Leukemias" and "Pipeline Insight: Lymphomas, Multiple Myeloma & Myelodysplastic Syndromes", March 2010.

CLL, DLBCL, FL prevalence based on median survival of 8 yrs: company estimates.

MM 2012 incidence: Datamonitor, "Multiple Myeloma Epidemiology", May 2013; MM prevalence: SEER 2012; company estimates.

MS incidence, "Atlas of MS 2013"

RRMS prevalence, Datamonitor, "Multiple sclerosis Epidemiology", May 2012.

Sales data for CLL, FL, MM based on EvaluatePharma® 2014, sales data for MS from Datamonitor, "Multiple Sclerosis Forecast", 3 February 2014.

<sup>&</sup>lt;sup>1</sup>Incidence for MS does not include Japan

<sup>&</sup>lt;sup>2</sup>Sales data is for NHL, which includes FL

<sup>&</sup>lt;sup>3</sup>Data is for MS, which includes RRMS

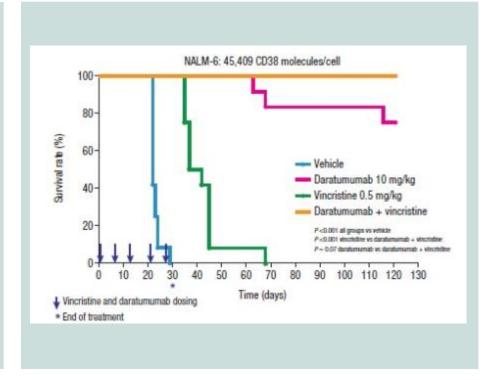


## Daratumumab Beyond Multiple Myeloma Pre-clinical Activity in DLBCL & ALL (EHA 2014)

# Effect daratumumab on tumor growth in patient-derived DLBCL model

# Tumor growth ST1361 DLBCL model 3,000 2,000 1,000 1,000 14 28 42 56 Day IgG control - Daratumumab - CHOP - R-CHOP - CHOP/Daratumumab - R-CHOP Daratumumab

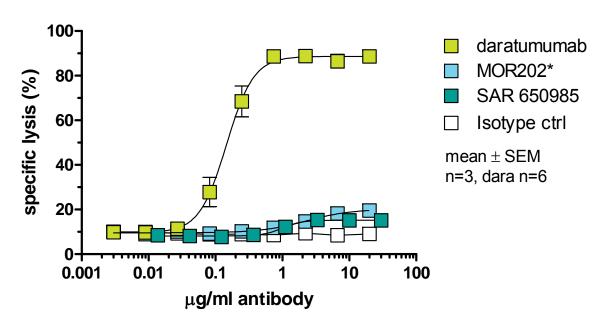
# Effect daratumumab with or without vincristine in ALL xenograft model



Data presented at EHA 2014 24



## **Daratumumab Induces Superior CDC**



	Daratumumab	MOR202* 1	SAR 650984 1, 2
	(Genmab)	(MorphoSys)	(Sanofi-Aventis)
EC50 (μg/mL)	0.15	2.3	1.0
Maximum killing (%)	90	20	15

<sup>\*</sup>MOR202 clone MOR03087; ¹:surrogate mAb produced in HEK cells, generated using VH and VL sequences as published PCT patent applications WO2012/041800 (MOR03087) and WO2008/047242 (38SB19); ²:38SB19



# CD38 Landscape

## In-house Comparison with Surrogates of MOR202 and SAR 650984

		Daratumumab (Genmab)	MOR202 <sup>1</sup> (MorphoSys)	SAR 650984 <sup>1, 2</sup> (Sanofi-Aventis)
	Origin	Human	Human	Humanized
	Development phase	Phase III	Phase I/IIa	Phase I/II
	Binding <sup>3</sup>	+++	++	+++
Mechanism of Action	ADCC (max lysis) <sup>3</sup>	++	++	++
	CDC (max lysis) <sup>3</sup>	+++	+	+
	Phagocytosis <sup>3, 4</sup>	+++	++	nd
	Ecto-enzyme function	+	nd	++
	Direct PCD 5, 6	-	-	++
	PCD after cross- linking <sup>5, 6</sup>	+++	+++	+++

<sup>\*</sup>MOR202 clone MOR03087; ¹:surrogate mAb produced in HEK cells, generated using VH and VL sequences as published in PCT patent applications WO2012/041800 (MOR03087) and WO2008/047242 (38SB19); ²:38SB19; ³:Daudi cells; ⁴:based on EC50 data, ⁵:Ramos cells ⁶: PCD: Programmed cell death, measured by Annexin V positivity and Caspase-3 activation. nd = not determined

Data presented at European Antibody Congress 2013, Nov. 2013 & 1st Annual Summit on Practical and Emerging Trends in Multiple Myeloma, March 2014 26



# Immuno-Oncology Turning Cancer into a Chronic Condition

#### Hottest Area in Oncology

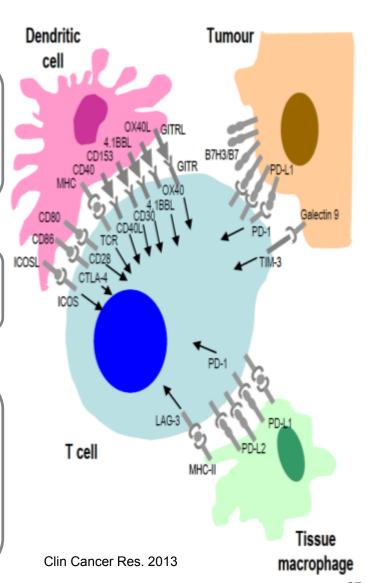
- Long duration of response
- Potential game changer
  - \$35B market

#### Many Immune Check Point Targets

Combinations may improve survival outcome

#### DuoBody

- Robust & versatile BsAb platform
- · Ideal for:
  - Screening multiple combinations in final therapeutic format
  - Combined targeting immune check points





# Positive Phase II Ofatumumab + Bendamustine Data in CLL

- 97 CLL patients in study
- Previously untreated CLL
  - 44 patients
  - 95% Overall response rate
  - 43% Complete response rate
    - 56% of these achieved MRD negativity in bone marrow or blood
- Relapsed CLL\*
  - 53 patients
  - 74% ORR
  - 11% CR
- Treatment was well tolerated\*\*



<sup>\*</sup>Unapproved indication

<sup>\*\*</sup>The most common adverse reactions (>20% of patients) were neutropenia, nausea, rash, pyrexia and thrombocytopenia.



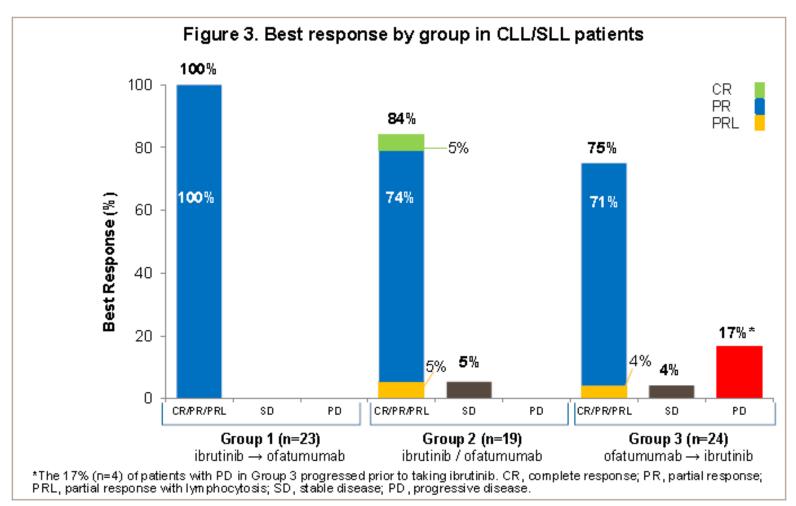
#### **Recent Ofatumumab News**

#### Phase III DLBCL H2H study & bulky fludarabinerefract. CLL study miss primary endpoint

- DLBCL: ORCHARRD study
  - 447 patients, 2 treatment arms: ofa + chemo vs. rtx + chemo
  - No statistically significant difference in PFS between treatment arms
  - Regulatory filing unlikely
- Bulky fludarabine-refract. CLL study
  - 122 patients, randomized 2:1 Ofa vs physicians choice
  - Median PFS assessed by IRC 5.36 months vs 3.61 months (p=0.267)
  - Of a performed broadly in line with previous data
  - · Post marketing obligation EU



# Ibrutinib -Ofatumumab Combination Highly Active Dosing Sequence Optimization Required



- ORR of 100% 75%
- PFS of 85% 90% at 12 months in distinct dosing sequence regimens



# Better Antibodies By Design

