



# Better Antibodies By Design

Jefferies London Healthcare Conference  
November 16, 2016



# 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.

# Transforming Cancer Treatment

## Focus



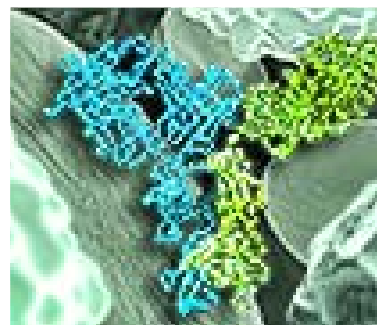
- Differentiated antibodies
- Treatment of cancer

## Products



- DARZALEX<sup>®</sup> approved in US & EU
- Arzerra<sup>®</sup> marketed globally
- 8 other antibodies in clinical studies
- Innovative pre-clinical pipeline

## Technologies



- DuoBody<sup>®</sup> platform
- HexaBody<sup>®</sup> technology

## Partnerships














- Leverage our technologies
- Strategic collaborations with pharma & biotech

# Innovative Clinical & Pre-clinical Pipeline

## Further Development for Marketed Products

Product	Disease Indications	Development Phase			
		Pre-clinical	I	II	III
<b>Daratumumab</b> Target: CD38 Partner: Janssen	<b>BTB (2)</b> Multiple myeloma (MM)				
	Non-Hodgkin's lymphoma (NHL)				
	Natural Killer /T-Cell Lymphoma (NKTCL), Nasal Type	Announced			
	Solid tumors	Announced			
<b>Ofatumumab</b> Target: CD20 Indication: Cancer Partner: Novartis	<b>BTB</b> Chronic lymphocytic leukemia (CLL)				
	Follicular lymphoma (FL)				
<b>Ofatumumab (OMB157)</b> Target: CD20 Indication: AI Partner: Novartis	Relapsing multiple sclerosis (RMS) (SubQ)				

# Innovative Clinical & Pre-clinical Pipeline - Continued

Product	Disease Indications & Target	Development Phase				
		Pre-clinical	I	I/II	II	III
<b>Tisotumab vedotin</b> Partner: Seattle Genetics	Solid Cancers, Target: TF					
➤ <b>20 Active Pre-clin. progr. incl. HuMax-AXL-ADC, HexaBody DR5/DR5, DuoBody CD3xCD20</b>	Proprietary programs: HuMab, HuMab-ADC, DuoBody, DuoBody-ADC & HexaBody					
	Partnered programs: HuMab, DuoBody & HexaBody					
<b>Teprotumumab (RV001)</b> <b>BTD</b> Partner: River Vision	Graves' orbitopathy, Target: IGF-1R					
<b>HuMax-TAC-ADC</b> Partner: ADCT	Lymphoma, Target: CD25					
	Acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL), Target: CD25					
<b>HuMax-IL8</b> Partner: BMS	Metastatic solid tumors, Target: IL-8					
<b>JNJ-61178104</b> Partner: Janssen	Autoimmune disorders, Target: inflammatory mediators					
<b>JNJ-61186372</b> Partner: Janssen	Non-small-cell lung cancer (NSCLC), Targets: EGFR, cMET					
<b>JNJ-63709178</b> Partner: Janssen	Acute Myeloid Leukemia (AML), Targets: CD3, CD123	<b>Clinical Hold</b> 				
<b>AMG 714</b> Partner: Celimmune (sublicensed from Amgen)	Celiac Disease, Target: IL-15					

# Daratumumab (Marketed as DARZALEX®)

Approved in US & EU as Fourth Line Treatment for MM Patients



First-in-class antibody targeting CD38

Marketed as monotherapy in US and EU for relapsed/refractory MM

2 FDA Breakthrough Therapy Designations

Clinical studies ongoing or announced in MM, NHL, NKT-cell lymphoma and solid tumors

Blockbuster potential – growing royalty income

Collaboration with Janssen Biotech



# Expansive Daratumumab Clinical Development

Indication	Disease Stage	Therapy	No. Pts*	Development Phase			
				I	I/II	II	III
Multiple Myeloma**	High Risk Smoldering	Mono	120	✓	SMM2001 (Centaurus)		
	Front line (transplant & non-transplant)	Dara + VMP	700	✓	MMY3007 (Alcyone)		
		Dara + Rd	730		MMY3008 (Maia)		
		Dara + VTd	1,080		MMY3006 (Cassiopeia)		
		Dara + RVd	216		MMY2004		
		Multi combo Study (6 arms)	250		MMY1001 (Equuleus)		
	Relapsed or Refractory	Dara + Rd	571	✓	MMY3003 (Pollux)		
		Dara + Vd	498	✓	MMY3004 (Castor)		
		Dara + K + Dex	450		Announced		
		Dara + Pom + Dex	155		H-35360		
		Subcutaneous	128		MMY1004 (Pavo)		
		Dara + Tecentriq	214		GO29695		
		Dara + durvalumab	138		FUSION MM003		
		Dara + Opdivo	375		CA209-039		
	NHL (DLBCL / MCL / FL)	Mono	210		LYM2001 (Carina)		
	NKTCL	Nasal Type	32		NKT2001 Announced		
	Solid Tumor	To be confirmed	100		Announced		

\*Approx. no. based on clinicaltrials.gov \*\*Maintenance integrated into some study protocols

V = bortezomib, MP = melphalan-prednisone, T = thalidomide, d= dexamethasone, R = lenalidomide

**Total:** >6,000

✓ Fully Recruited

Select Studies

# Efficacy in Monotherapy

## Combined Analysis of Monotherapy Studies

### Daratumumab as a single agent

- Approved by FDA and conditionally approved by EMA in relapsed/refractory multiple myeloma<sup>1,2</sup>

### Patients received a median of 5 prior lines of therapy

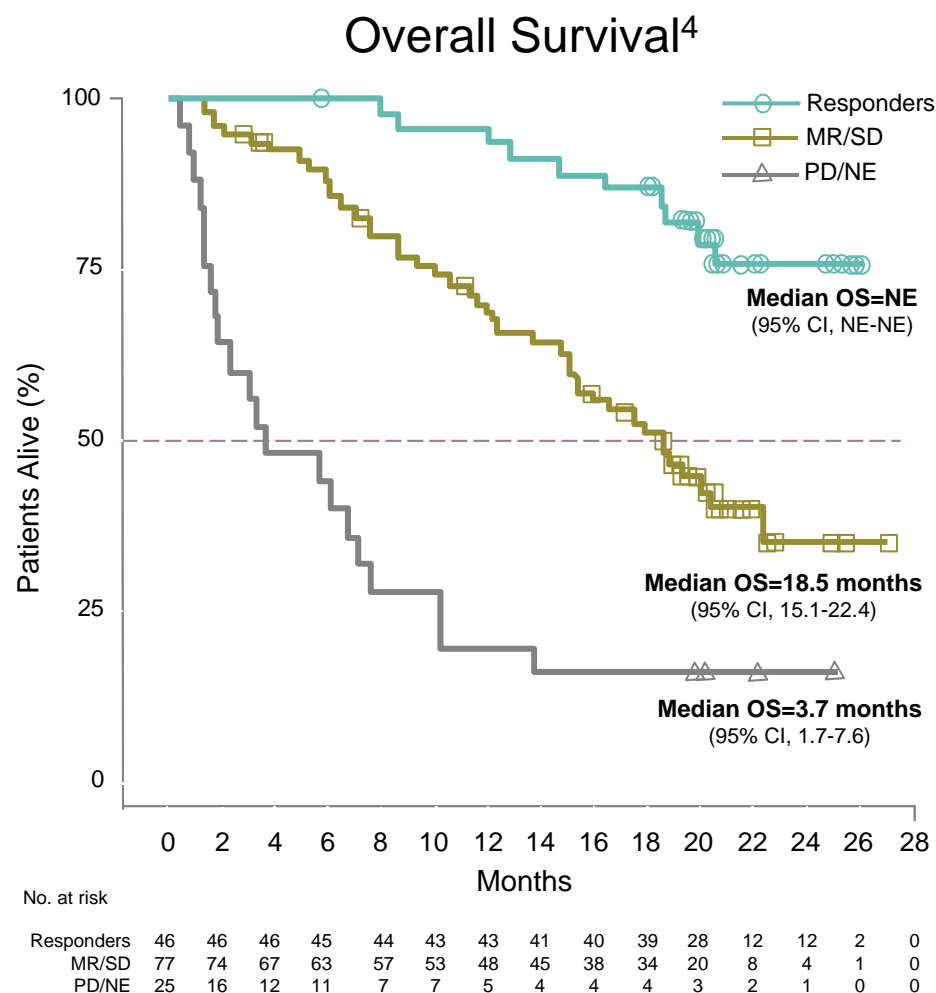
- 86.5% of patients were double refractory to a proteasome inhibitor (PI) and immunomodulatory drug (IMiD)<sup>3</sup>

### Median overall survival (OS): 20.1 months<sup>3</sup>

- 2-year OS was ~75% in responders
- Median OS was 18.5 months MR/SD patients

**ORR = 31%<sup>3</sup>**

**ORR was consistent in subgroups including age, number of prior lines of therapy, refractory status, or renal function**



MR, minimal response; SD, stable disease; PD, progressive disease; OS, overall survival; CI, confidence interval; NE, not evaluable.

1. Lokhorst HM, et al. *N Engl J Med*. 2015;373:1207-19.

2. Lonial S, et al. *Lancet*. 2016;387:1551-60.

3. Usmani SZ, et al. *Blood*. 2016;128(1):37-44

4. Data presented at ASCO 2016



# Two Phase III Studies Hit Primary Endpoint at Interim Relapsed or Refractory Multiple Myeloma: CASTOR

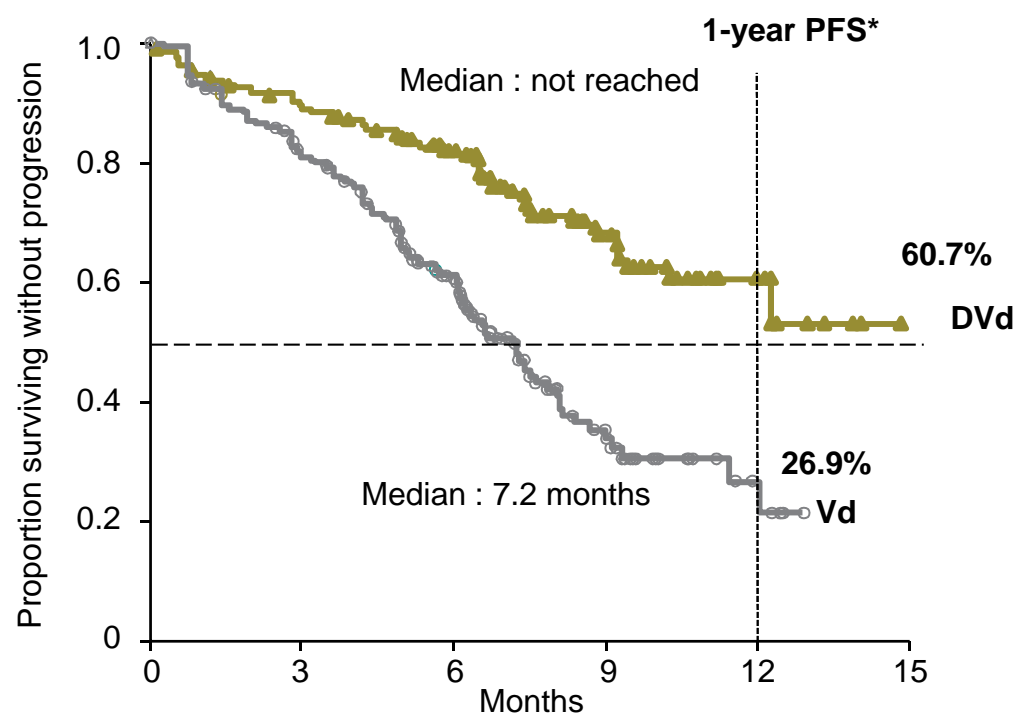
## CASTOR

**Dara + Bort + Dex  
(DVd)**

Hazard Ratio=0.39  
( $P < 0.0001$ )

	DVd	Vd
ORR	83%	63%
≥ VGPR	59%	29%
≥ CR	19.2%	9%
PFS	NR	7.2 mo

## CASTOR Kaplan-Meier Plot - PFS



No. at risk						
Vd	247	182	106	25	5	0
DVd	251	215	146	56	11	0

\*KM estimate

Presented at ASCO Plenary session – Chicago, June 5

# Two Phase III Studies Hit Primary Endpoint at Interim Relapsed or Refractory Multiple Myeloma: POLLUX

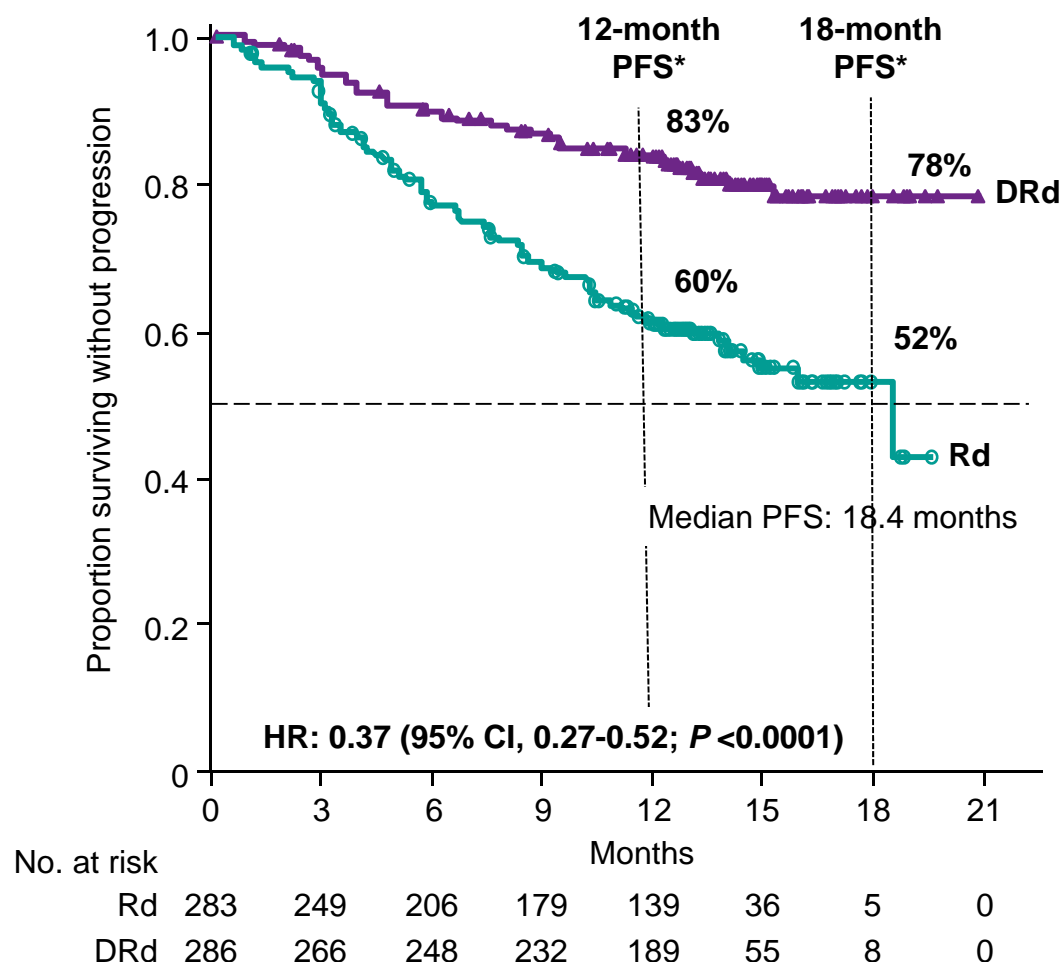
## POLLUX

**Dara + Len + Dex  
(DRd)**

Hazard Ratio=0.37  
( $P < 0.0001$ )

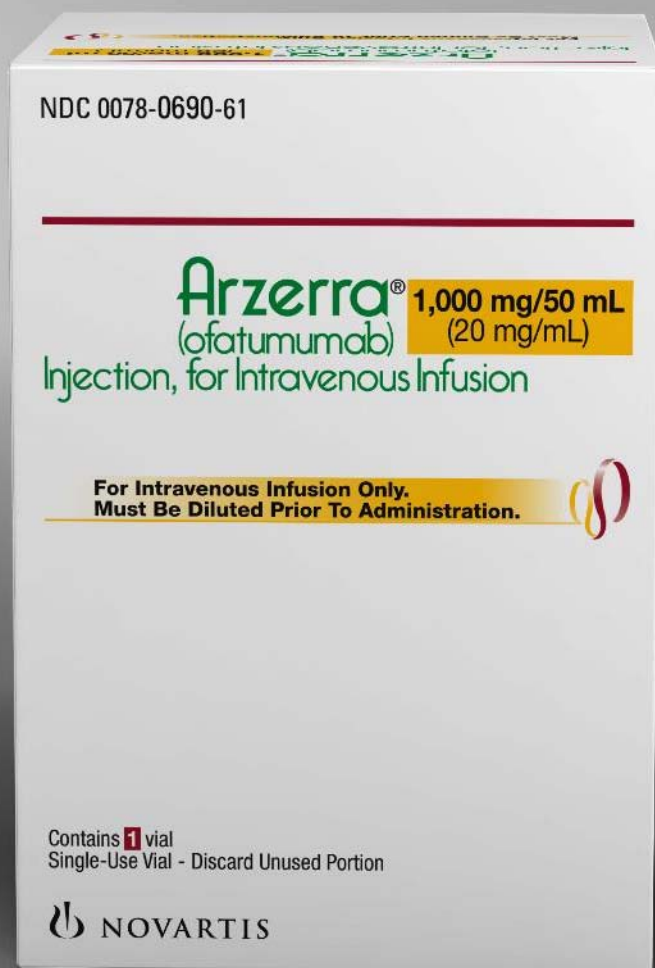
	DRd	Rd
ORR	93%	76%
$\geq$ VGPR	76%	44%
$\geq$ CR	43%	19%
PFS	NR	18.4 mo

## POLLUX Kaplan-Meier Plot - PFS



Presented at EHA Copenhagen, June 10

# Ofatumumab (Arzerra®)



Human antibody targeting CD20

New Phase III studies in relapsing MS started

Marketed in various territories for certain CLL indications\*

Phase III studies ongoing in CLL and iNHL

Collaboration with Novartis

Cash flow positive for Genmab

\*See local country prescribing information for precise indications

# Tisotumab vedotin: Next Generation Therapeutic

## Phase I/II & Phase I studies in Patients with Solid Tumors



Fully human antibody-drug conjugate (ADC)

Targets Tissue Factor (TF)

Therapeutic potential in broad range of solid tumors

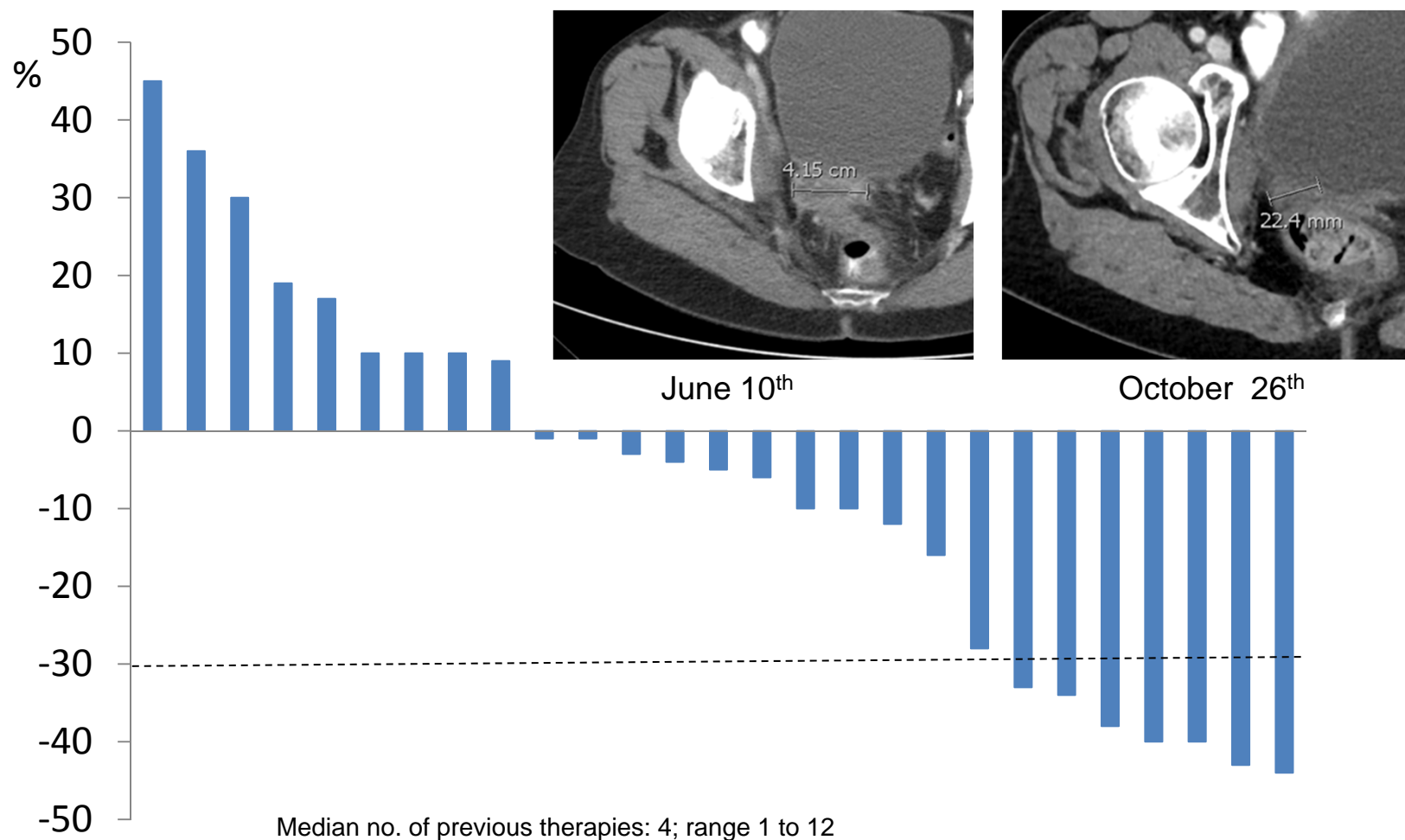
2 Phase I/II studies ongoing in solid tumors

Encouraging preliminary safety & efficacy data

Collaboration with Seattle Genetics

# Early and Preliminary Efficacy – GEN701 Part 2

## Best % Change (RECIST) from Baseline



# Next in the Clinic: HuMax-AXL-ADC

## Efficacy in *in vivo* Tumor Model



Human ADC

Targets the tumor-associated antigen AXL

Therapeutic potential in solid tumors

First-in-human Phase I/II study

ADC technology licensed from Seattle Genetics

# Cutting Edge Proprietary Technologies

## Creating Truly Differentiated Products

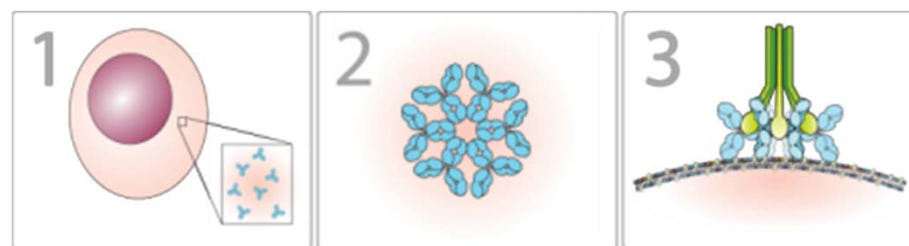


### DuoBody

- Efficient & versatile bispecific Ab platform
- Applicable to any antibody from any platform
- Regular IgG format
- Large scale production validated
- No developability liabilities
- Robotized bispecific library generation
- Multiple ongoing collaborations incl. with Novartis, Novo Nordisk, Gilead & Janssen Biotech

### HexaBody

- Robust effector function enhanced Ab
- Enables antibodies to readily form clusters of 6 (hexamers)
- Induces & enhances target cell killing after binding (CDC and apoptosis)
- Creates innovative products in cancer & infectious diseases
- Collaborations with Humabs BioMed, Agenus and others





# Genmab Proprietary Knock-Your-Socks-Off Pipeline

## Potential INDs in next 4 years

Technology	product	2016	2017	2018	2019	2020
ADC	HuMax-AXL-ADC	✓				
HexaBody	HexaBody-DR5/DR5					
DuoBody	DuoBody-CD3xCD20					
HexaBody	HexaBody-X					
DuoBody-ADC	DuoBody-XxY-ADC					
DuoBody	DuoBody-CD3xX					
Immuno-Oncology [>10 progr.]*	DuoBody-A					
	DuoBody-B					
	DuoBody-C					
	DuoBody-D					
	DuoBody-E					

\*: Aduro Biotech & BioNTech

Pre-clinical pipeline targeting at least 4 leapfrog INDs in next 4 years

# HexaBody-DR5/DR5

## Targeting DR5 for Cancer Therapy

### DR5 (death receptor 5)

Cell surface receptor that mediates programmed cell death

In normal physiology, binding of TRAIL ligand results in DR5 clustering & cell death

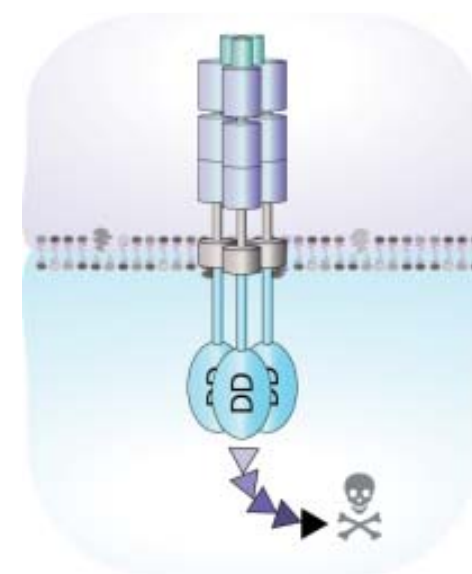
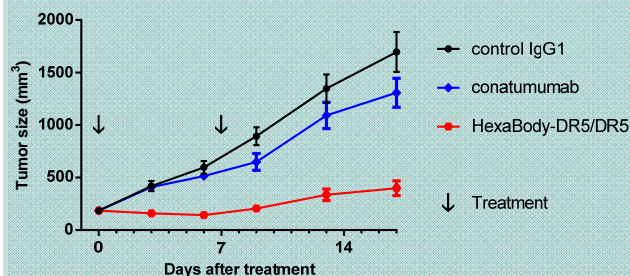


### Targeting DR5 for treatment of cancer

- Agonistic DR5 mAb induce apoptosis after crosslinking
- Agonistic DR5 antibodies have shown limited anti-tumor activity in the clinic

- Need for increased therapeutic potency
- Use HexaBody technology to induce clustering & activation of DR5 molecules, without a need for additional crosslinking
- Combination of two HexaBody molecules against two non-overlapping DR5 epitopes induces maximal cell death

#### Mouse xenograft model



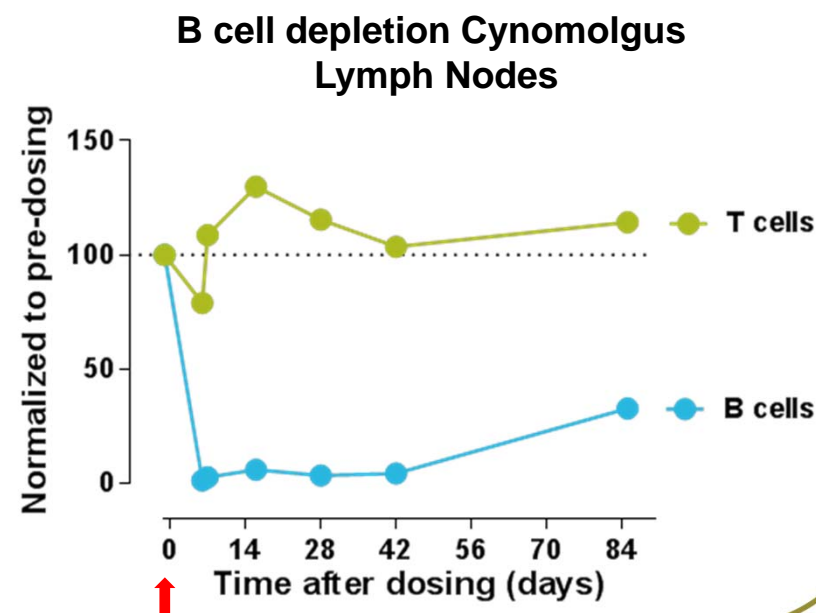
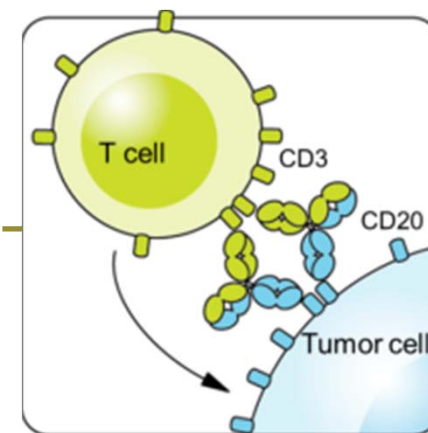
DR5 activation induces cell death

# DuoBody CD3xCD20

## Key Characteristics

### Humanized IgG1 bispecific antibody

- DuoBody platform
- Regular half life
- Non-activating Fc-domain
- Potently activates T cells to kill CD20<sup>+</sup> tumor cells
- Cynomolgus CD3 & CD20 x-reactive
  - Potent Cynomolgus B cell depletion (peripheral blood, lymph nodes)
- 2017 IND candidate



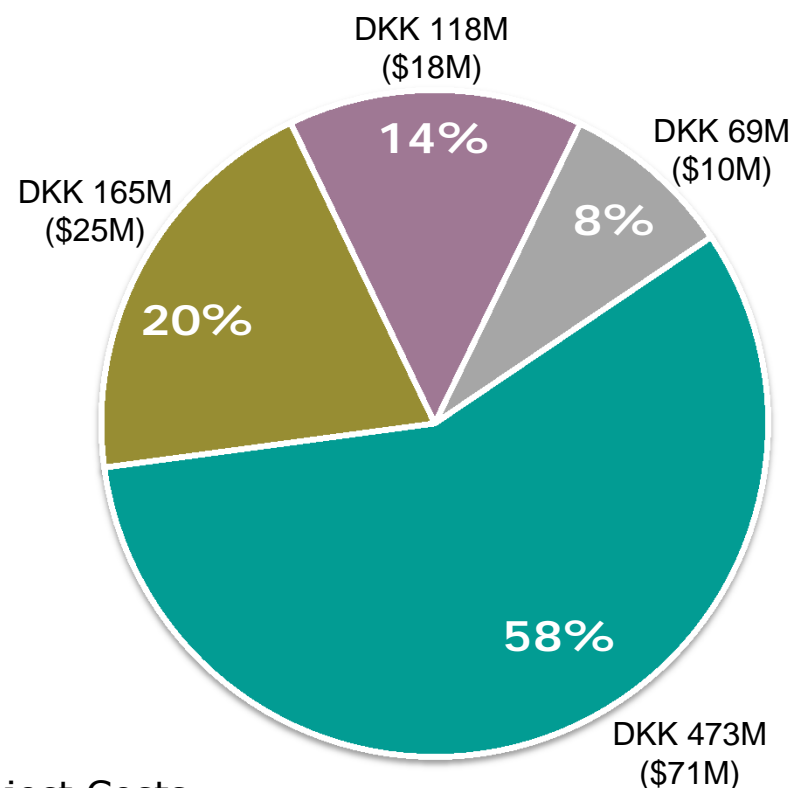
# Well-Capitalized Biotech – 2016 Guidance

Income Statement	DKKM	USDM*
Revenue	1,200 – 1,250	180 - 187
Operating expenses	(800) – (850)	(120) – (127)
Operating income	375 - 425	56 - 64
Cash position at end of year**	3,650 – 3,750	547 - 562
*USD 1.00 = DKK 6.6762 (Sept 30, 2016)		
**Cash, cash equivalents and marketable securities		

2016 Guidance – Nov 2, 2016

- Largest increase in expenses (over 2015) is in development
  - Driven by additional investment in pipeline products
  - Total 2016 spend on 4 key products is ~DKK 319M or 39% of total expense
- Additional investment in pre-clinical pipeline

## 2016 Expense Base DKK 825M (\$124M)



- Project Costs
- Salaries
- Support Svcs
- Depr. & Stock Comp.

# Creating Value for Patients and Shareholders



## Daratumumab

- Approved in RRMM
- Studies across all MM indications
- Studies in new indications planned
- Significant market potential



## Ofatumumab

- New opportunity in relapsing Multiple Sclerosis
- Approved in certain types of CLL

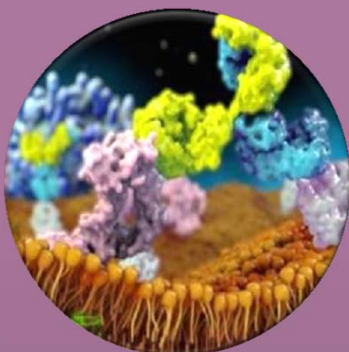


## Two proprietary next generation clinical programs

- Promising early tisotumab vedotin data
- HuMax-AXL-ADC now in the clinic

Value Creation

# Creating Value for Patients and Shareholders



## Novel differentiated drug candidates

- DuoBody-CD3xCD20 – '17 IND candidate
- HexaBody-DR5/DR5; broad potential in cancer – '17 IND
- DuoBody Immuno-Oncology programs with partners



## Innovation powerhouse

- World class antibody expertise
- Inspired by nature
- Inventing tomorrow's differentiated medicines via next generation antibody technologies



## Positioned for success

- Substantial earnings potential
- Able to robustly invest in & accelerate future pipeline
- Building commercial capabilities

**Value Creation**



## 2016 Goals: Maximizing Product Portfolio Value

Priority	✓	Targeted Milestone
Maximize daratumumab progress	<div>✓</div> <div>✓</div> <div>✓</div> <div>✓</div> <div>2017*</div>	» Launch DARZALEX™ in US and other approved territories » CHMP decision on monotherapy application » Phase III multiple myeloma (MM) interim efficacy analysis in relapsed / refractory MM settings [Pollux and Castor trials] » File for label in relapsed / refractory settings if results of interim analyses are favorable » Start multiple clinical trials in MM and non-MM indications » Report initial clinical data non-MM indications
Optimize ofatumumab value	<div>✓</div> <div>✓</div> <div>2017+</div>	» Start Phase III sc autoimmune trials » Regulatory decision for CLL maintenance » File for label in relapsed CLL » Phase III refractory follicular lymphoma (FL) interim efficacy data
Strengthen differentiated product pipeline	<div>✓</div> <div>✓</div>	» Phase I tisotumab vedotin additional data » IND for HuMax-AXL-ADC and start clinical trial » Progress HexaBody-DR5/DR5 program » Progress pre-clinical DuoBody & HexaBody projects
Broaden partnership portfolio with next generation technologies	<div>✓</div> <div>✓</div>	» Sign new / expanded DuoBody & HexaBody collaborations » Progress partnered programs » New IND filings
Disciplined financial management		» Selectively invest to progress and broaden differentiated product pipeline

\*Clinical data from a non-MM indication for daratumumab is now anticipated in 2017

+Study continued at interim analysis. Full data expected 2017.



## Creating Value for Patients and Shareholders



### Building on 3 central pillars: Focus, Innovation & Execution

- 2 marketed products
- 2 early stage clinical programs
- 2 proprietary technologies
- Robust pre-clinical pipeline
- Unique Antibody & R&D expertise
- Strategic collaborations
- Building commercial expertise
- Solid financials
- Proven track record



*Innovating  
antibodies,  
improving lives*

# Better Antibodies By Design

