# ALLIGATOR bioscience

## **Company presentation**

### Per Norlén CEO, CMO

Carnegie Healthcare Seminar 17 March 2016

Strictly private and confidential

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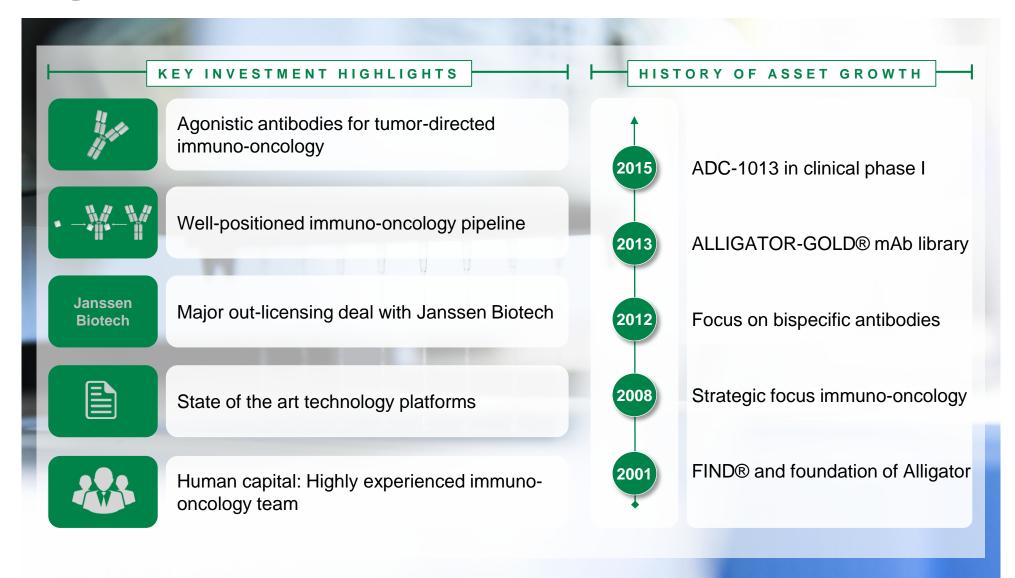
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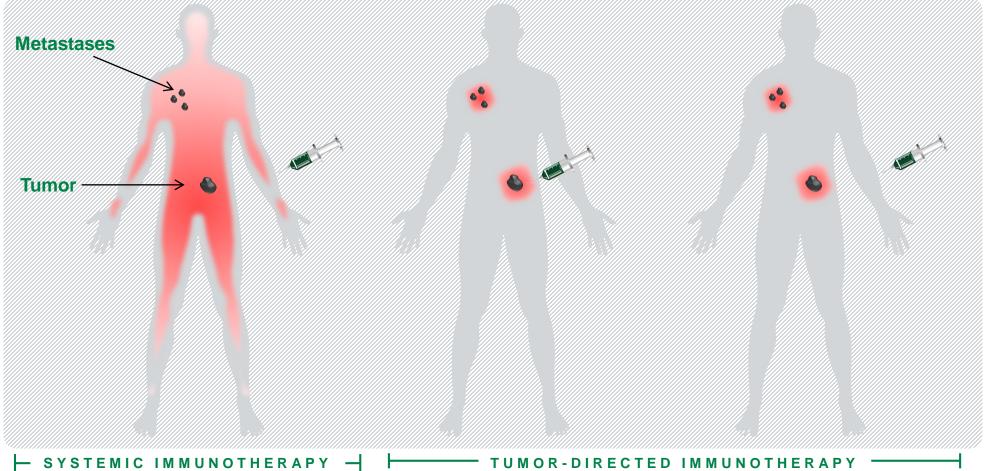


### **Alligator Bioscience in brief**





### **Tumor-directed immuno-oncology**



General immune activation with potential severe toxicity

**TUMOR-DIRECTED IMMUNOTHERAPY** 

#### **INTRA-TUMORAL INJECTION**

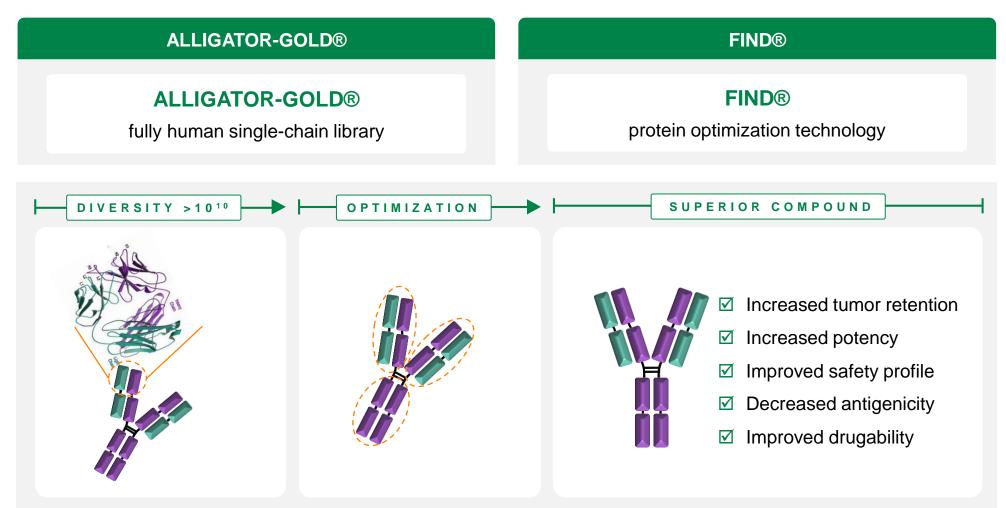
Tumor-selective immune activation with less systemic toxicity

#### **TUMOR-LOCALIZING ANTIBODIES**

Tumor-selective immune activation with less systemic toxicity



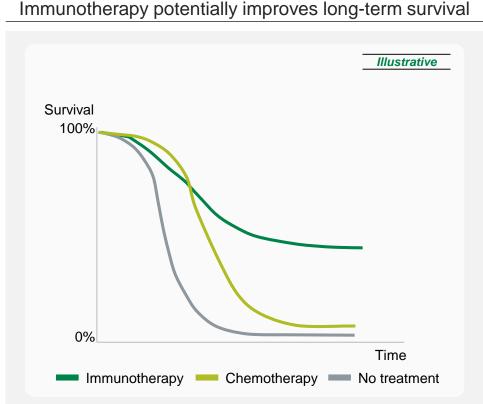
### Fully integrated technology platforms



Technology platforms will enable Alligator to continue to develop innovative antibodies for years to come

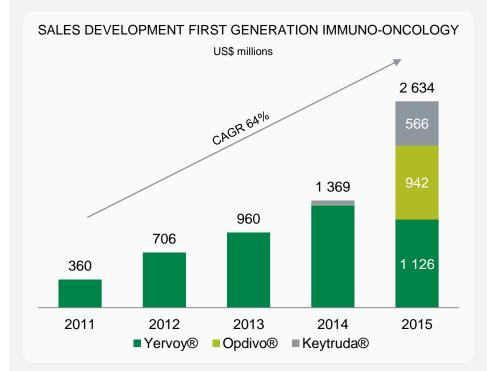


### Rapid development within the field of immuno-oncology



#### Immuno-oncology is shifting treatment response towards durable survival

 Substantial market potential as virtually any type of cancer can potentially be treated by immunotherapy Strong uptake in first generation products



- Yervoy® (CTLA-4 inhibitor), Opdivo® (PD-1 inhibitor) and Keytruda® (PD-1 inhibitor)
- Several ongoing clinical trials for label extensions of first generation

Market potential for immuno-oncology drugs estimated at US\$ ~30 billion annually



### Well-positioned and promising drug development pipeline

Development pipeline focusing on agonistic monospecific and bispecific antibodies targeting TNFR superfamily

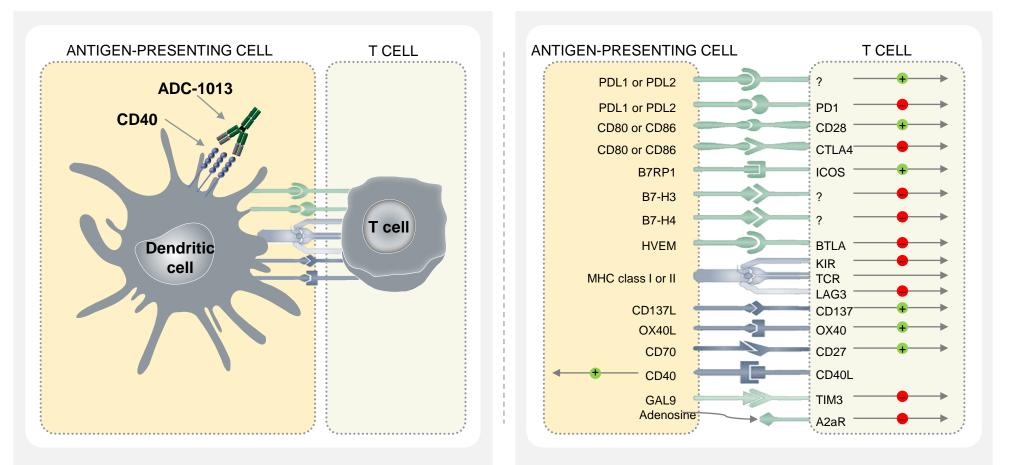
PROJECT	MOLECULE	TARGET	LEAD OPTIMIZATION	POC IN-VIVO	PRE-CLINICAL	PHASE I	PHASE II
ADC-1013	Monospecific	CD40					
ADC-1015	Bispecific	OX40/CTLA-4					
ADC-1016	Bispecific	TNFR superfamily + TAA					
Research projects	Monospecifics	TNFR superfamily					
Research projects	Bispecifics	TNFR superfamily + ND		- - - - - -			



### ADC-1013: CD40 is a key immuno-oncology target

#### ADC-1013 Mode of Action

Co-stimulating receptors



CD40 is the only defined receptor that selectively activates the antigen-presenting cell and is a highly promising target for combination with T-cell activating antibodies such as PD-1 and CTLA-4



## ADC-1013: Antibody based immuno-oncology drugs in clinical development

Selection of antibody based immuno-oncology drugs in clinical development

Company	Drug	Indication	Phase	Target
Roche (Genentech)	atezolizumab	NSCLC, bladder, renal, etc		PD-L1
AstraZeneca (MedImmune)	durvalumab	NSCLC, H&N, bladder	III	PD-L1
Pfizer & AstraZeneca	tremelimumab	Mesothelioma, NSCLC, etc	III	CTLA-4
Pfizer & MerckSerono	avelumab	NSCLC, GI, bladder	III	PD-L1
Prima Biomed (Immutep)	IMP-321	Breast cancer	III	LAG3
CureTech	pidilizumab	BCL, NHL, melanoma, CRC	II	PD-1
Novartis	PDR-001	NSCLC, CRC, GI, etc	II	PD-1
AstraZeneca (MedImmune)	MEDI-0680	BCL, NHL, melanoma, CRC	II	PD-1
AgonOx (AstraZeneca)	MEDI-6469	Breast, prostate, lymphoma	II	OX40
Bristol-Myers Squibb	urelumab	Solid tumors and lymphomas	II	CD137
Novartis	LAG-525	Solid tumors	II	LAG3
Bristol-Myers Squibb	BMS-986156	Solid tumors	II	GITR
Celldex	varlilumab	Solid tumors	II	CD27
Alligator Bioscience	ADC-1013	Solid tumors		CD40
Apexigen	APX-005M	Lymphoma		CD40
Roche	RG-7876	Solid tumors	I	CD40
Seattle Genetics	SEA-CD40	Solid tumors		CD40
Bristol-Myers Squibb	BMS-986016	Solid tumors and lymphomas	I	LAG3
Novartis (Immutep)	IMP-701	Cancer	I	LAG3
Pfizer	PFE-1, PF-05082566	Solid tumors, Lymphomas	I	CD137
Merck	MK-4166	Solid tumors	I	GITR
AstraZeneca	MEDI-1873	Solid tumors	I	GITR
AstraZeneca	MEDI-6383	Solid tumors	I	OX40
Roche	MOXR-0916	Cancer	I	OX40
AstraZeneca	MEDI-0562	Cancer	I	OX40
GlaxoSmithKline	GSK-3174998	Cancer	I	OX40
Pfizer	PF-04518600	Cancer	I	OX40
Bristol-Myers Squibb	MDX-1105	Solid tumors	I	PD-L1
Regeneron	REGN-2810	Solid tumors, BCL	I	PD-1
BeiGene	BGB-A317	Cancer	I	PD-1

Approximately 70 immuno-oncology mAbs in clinical development

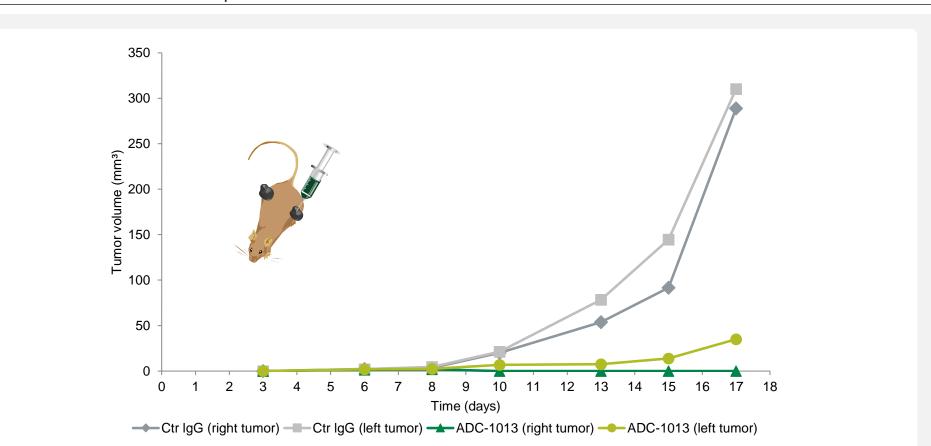


### ADC-1013: Systemic anti-tumor effects (1/2)





### ADC-1013: Systemic anti-tumor effects (2/2)



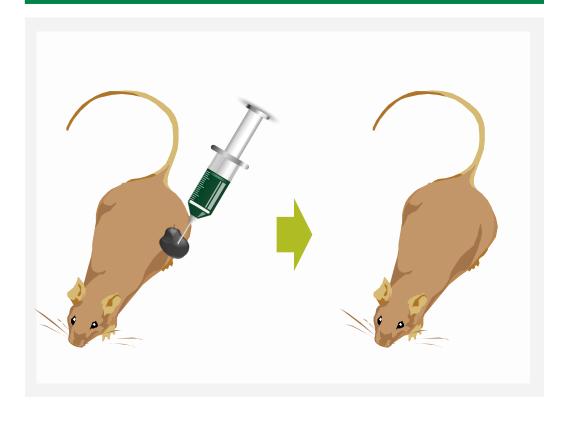
Results from pre-clinical evaluation of ADC-1013 in treatment of B16 melanoma

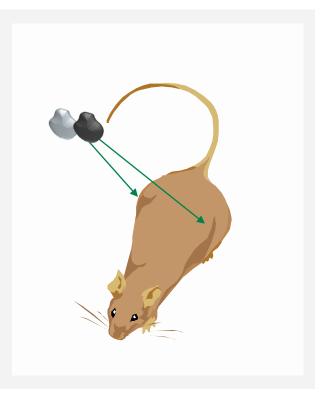
Local ADC-1013 treatment of one tumor (B16 melanoma) in hCD40tg mice delays growth of both the treated and the untreated tumor. Rapid tumor growth is seen of the two tumors in control mice.



### ADC-1013: Long term immunity (1/2)

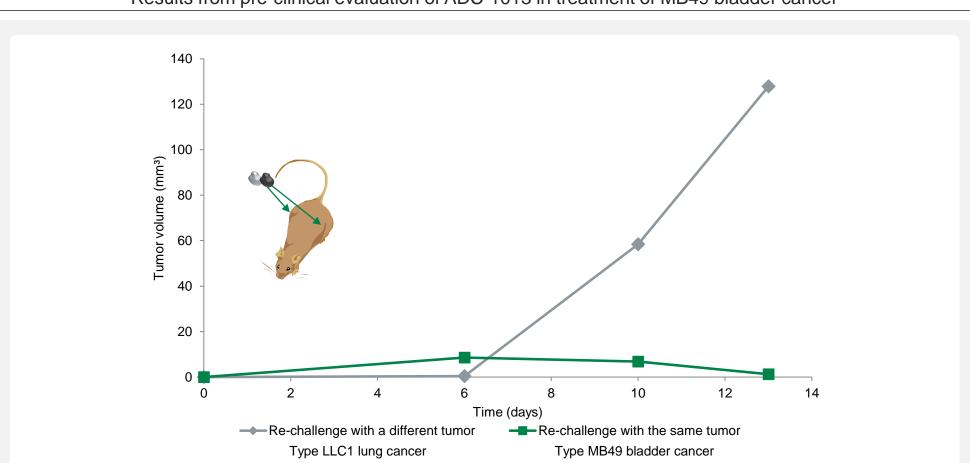
Mice can be cured from bladder cancer (MB49) by ADC-1013 in hCD40tg mice Cured mice are re-challenged with MB49 and LLC1, but receives no treatment







### ADC-1013: Long term immunity (2/2)



Results from pre-clinical evaluation of ADC-1013 in treatment of MB49 bladder cancer

Mice cured from MB49 are immune to later re-challenge with MB49 but not to re-challenge with LLC1

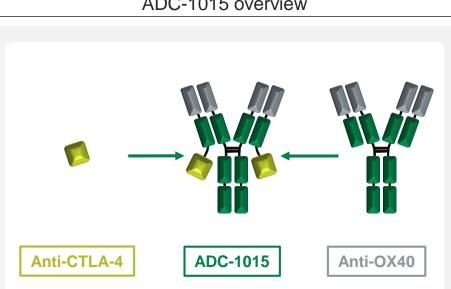


### **ADC-1013: Partnership validating Alligator's model**

#### Partnership details for ADC-1013 Description of ongoing Phase I trial 40 patients with → advanced solid tumors Janssen PHARMACEUTICAL COMPANIES 5 clinical sites in the OF Johnson Johnson UK, DK and SE **Description of agreement Royalty / Milestone potential Dosing &** Secondary Primary administration endpoint endpoints Exclusive world-wide Up-front payment plus additional milestones up to license to develop and commercialize ADC-1013 a potential total of US\$700 Pharmacokinetics FiH, first dose Safety and million April 2015 tolerability Alligator continues as Immunogenicity sponsor for the ongoing Tiered royalties on Dose escalation Phase I clinical trial worldwide net sales upon Clinical efficacy successful launch Intra-tumoral Extension and future studies to be sponsored by Janssen Extension of clinical scope to systemic administration



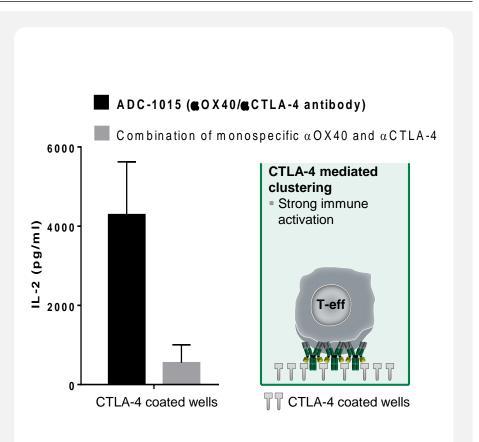
### ADC-1015: Bispecific OX40/CTLA-4 Ab in pre-clinical development



### ADC-1015 overview

- Bispecific antibody combining OX40 with CTLA-4
- Aim to induce superior efficacy through synergistic immune activation
  - Depletion and suppression of Treg \_
  - Activation of Teff
- Pre-clinical program ongoing

### Clustering results in superior efficacy (T-cell activation)



The effect of the bispecific antibody is superior to the effect of the combination of the monospecific antibodies - the effect is cross-linking dependent



### **Alligator highlights**

Agonistic antibodies for tumor-directed immunooncology

Well-positioned immuno-oncology pipeline

Major out-licensing deal with Janssen Biotech

State of the art technology platforms

Human capital: Highly experienced immunooncology team



ALLIGATOR