



## Company presentation

*Biotech Showcase, San Fransisco, 10 January 2017*

Per Norlén, CEO

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# Alligator Bioscience in brief

## COMPANY HIGHLIGHTS



Development of tumor-directed immuno-oncology antibodies to out-license after POC



Fast growing market for immuno-oncology drugs with estimated US\$ +30 billion potential



Well-positioned development pipeline of innovative immuno-oncology drugs

**Janssen  
Biotech**

Strategic partnership with Janssen worth US\$ +695 million



Solid intellectual property portfolio and state of the art technology platforms



Highly experienced BoD, management and research team within immuno-oncology

## HISTORY OF ASSET GROWTH

2015

ADC-1013 entering clinical phase I and major out-licensing deal

2013

ALLIGATOR-GOLD® mAb library

2012

Focus extended to bispecific antibodies

2008

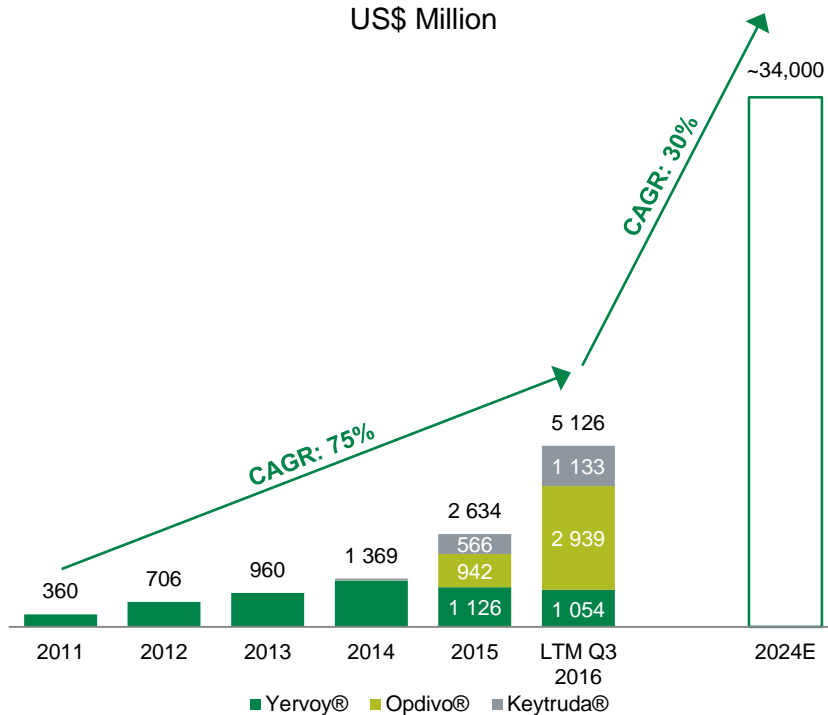
Focus on immuno-oncology

2001

FIND® and foundation of Alligator

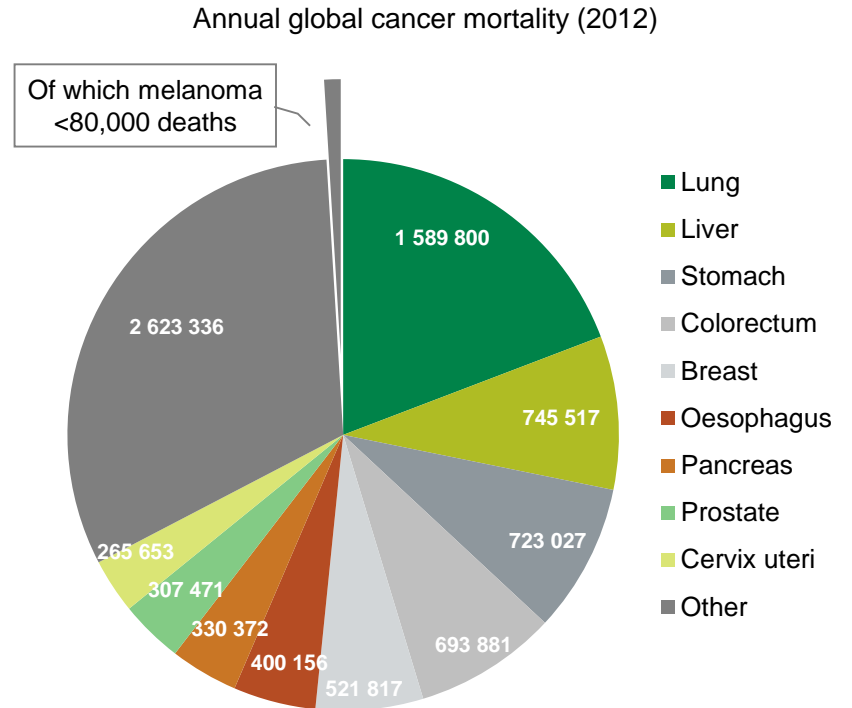
# Rapid uptake and development within the field of immuno-oncology

Sales of existing immuno-oncology treatments



Existing drugs showing strong uptake despite a high treatment price and relatively few cancer indications on label

Market potential for immuno-oncology



With 8,201,030 global cancer deaths annually, immuno-oncology has significant potential to grow to one of the largest therapy areas

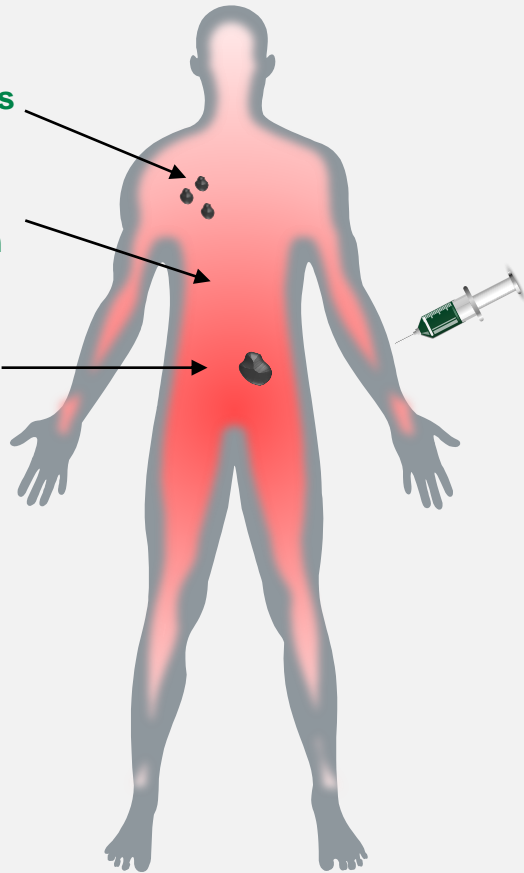
Consensus estimates the I-O market to hold the largest upside potential within the global pharmaceutical market

# Introduction to tumor-directed immuno-oncology

Metastases

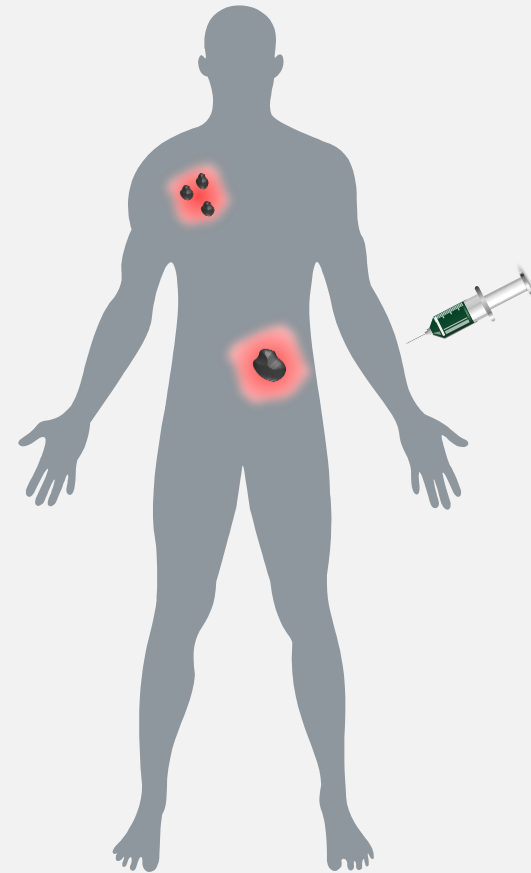
Immune  
activation

Tumor



## SYSTEMIC IMMUNO-ACTIVATION

Systemic administration of immunotherapeutic drugs results in general activation of the immune system, which may lead to severe side effects



## TUMOR-DIRECTED IMMUNO-ACTIVATION

Selective activation of tumor-specific immune cells results in a systemic immune-mediated anti-tumor attack with limited toxicity.

# Fully integrated technology platforms

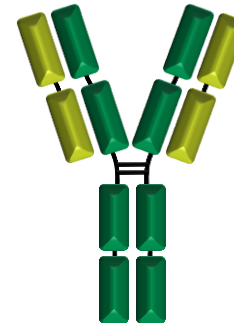
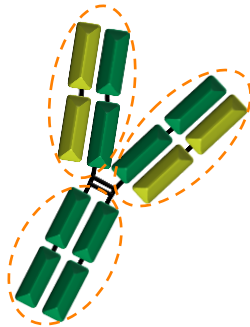
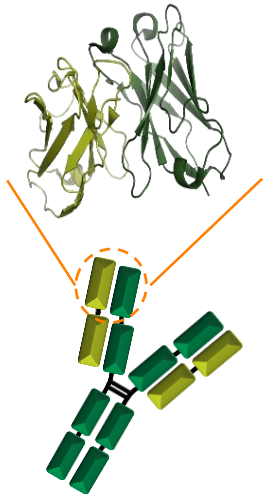
## ALLIGATOR-GOLD®

**ALLIGATOR-GOLD®** is a fully human single-chain library with large diversity

## FIND®

The **FIND®** technology is used to optimize antibodies and other proteins characteristics

— DIVERSITY > 10<sup>10</sup> — OPTIMIZATION — IMPROVED PRODUCT CANDIDATE —











- ✓ Increased tumor retention
- ✓ Increased affinity
- ✓ Improved safety profile
- ✓ Decreased antigenicity
- ✓ Improved developability

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



# Extensive collaboration with distinguished immuno-oncologists

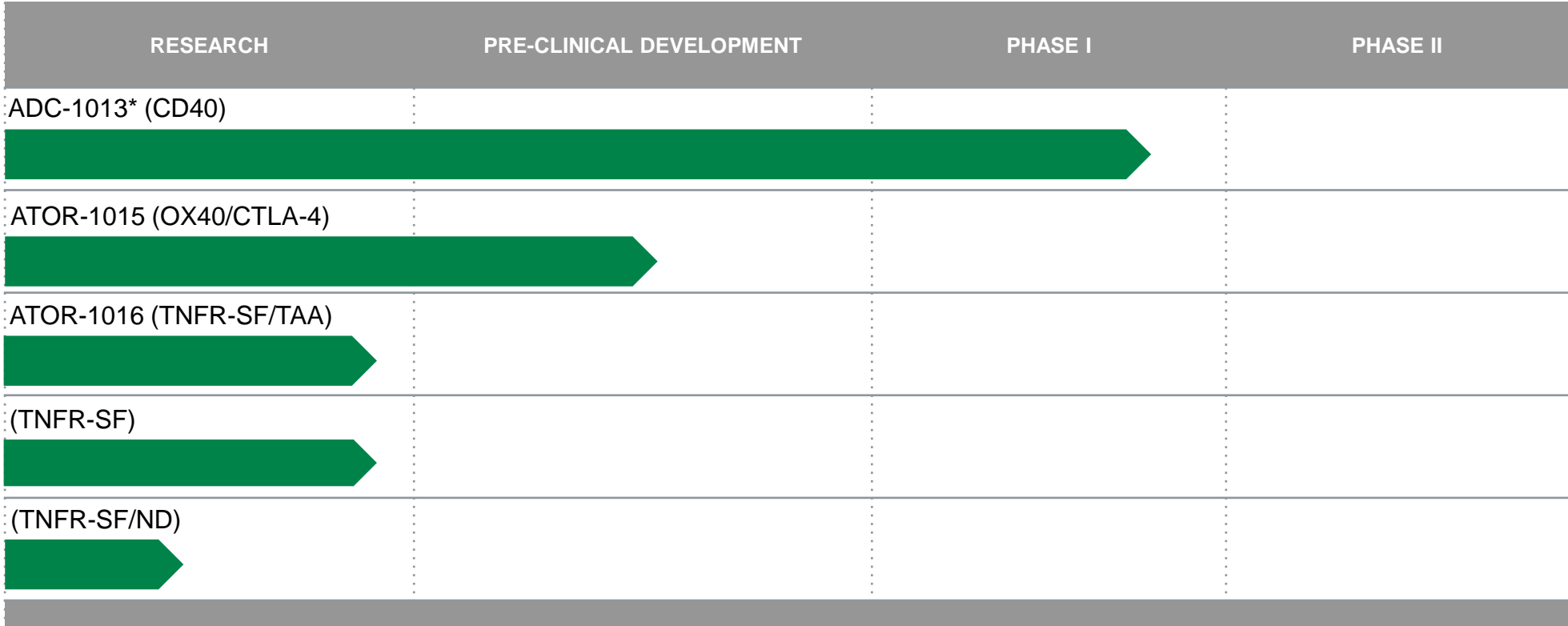
## Partners and major deliverables

Stanford University	Navarra University	Lund University	Uppsala University	University of Manchester	EU/TIMCC	The Royal Institute of Technology
<ul style="list-style-type: none"> <li>Pre-clinical In-vivo proof of concept supporting ADC-1015 and research programs</li> </ul>	<ul style="list-style-type: none"> <li>In-vitro and in-vivo characterization of Alligator compounds supporting ADC-1016 and research programs</li> </ul>	<ul style="list-style-type: none"> <li>DC and T-cell assays used for characterization of ADC-1013</li> <li>Next generation sequencing</li> </ul>	<ul style="list-style-type: none"> <li>In-vivo proof of concept (ADC-1013)</li> <li>Supporting research programs</li> </ul>	<ul style="list-style-type: none"> <li>Characterization of tumor targeting antibodies supporting ADC-1016 and research programs</li> </ul>	<ul style="list-style-type: none"> <li>Academic network of 6 leading groups from European Universities</li> <li>To characterize the tumor infiltrating myeloid cell compartment</li> </ul>	<ul style="list-style-type: none"> <li>Identification and characterization of novel immune modulating targets</li> </ul>
<div> <div>  <p><b>IGNACIO MELERO</b> MD, PhD, Professor</p> <p>Expert in pre-clinical and clinical tumor-directed and systemic immunotherapy</p>  </div> <div>  <p><b>THOMAS TÖTTERMAN</b> MD, PhD, Professor</p> <p>Pioneer in the field of tumor-directed immunotherapy</p>  </div> <div>  <p><b>PETER L. STERN</b> PhD, Professor</p> <p>Expert in tumor targets for cancer immunotherapy</p>  </div> <div>  <p><b>JEFFREY WEBER</b> MD, PhD, Professor</p> <p>Expert in clinical immuno-oncology</p>  </div> </div>						

Alligator will strive to increase the number of collaborations with both universities and small to mid-size biotechs

# Well-positioned drug development pipeline

Pipeline of immuno-stimulating mono- and bi-specific antibodies targeting TNFR superfamily



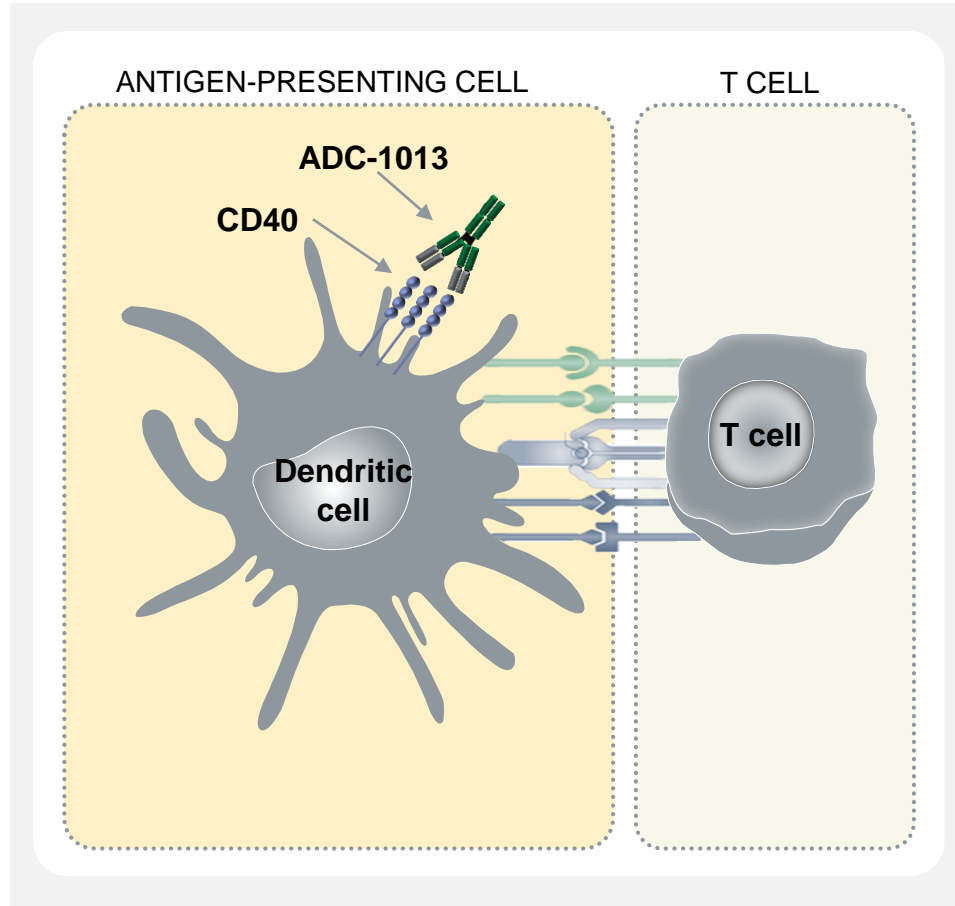
TNFR-SF: Tumor Necrosis Factor Receptor-Superfamily  
TAA: Tumor-Associated Antigen  
ND: Not Disclosed  
\*Partnered with Janssen Biotech Inc., developed as JNJ-64457107

All product candidates suitable for combination therapy with other I-O drugs, e.g. anti-PD-1 and anti-PD-L1

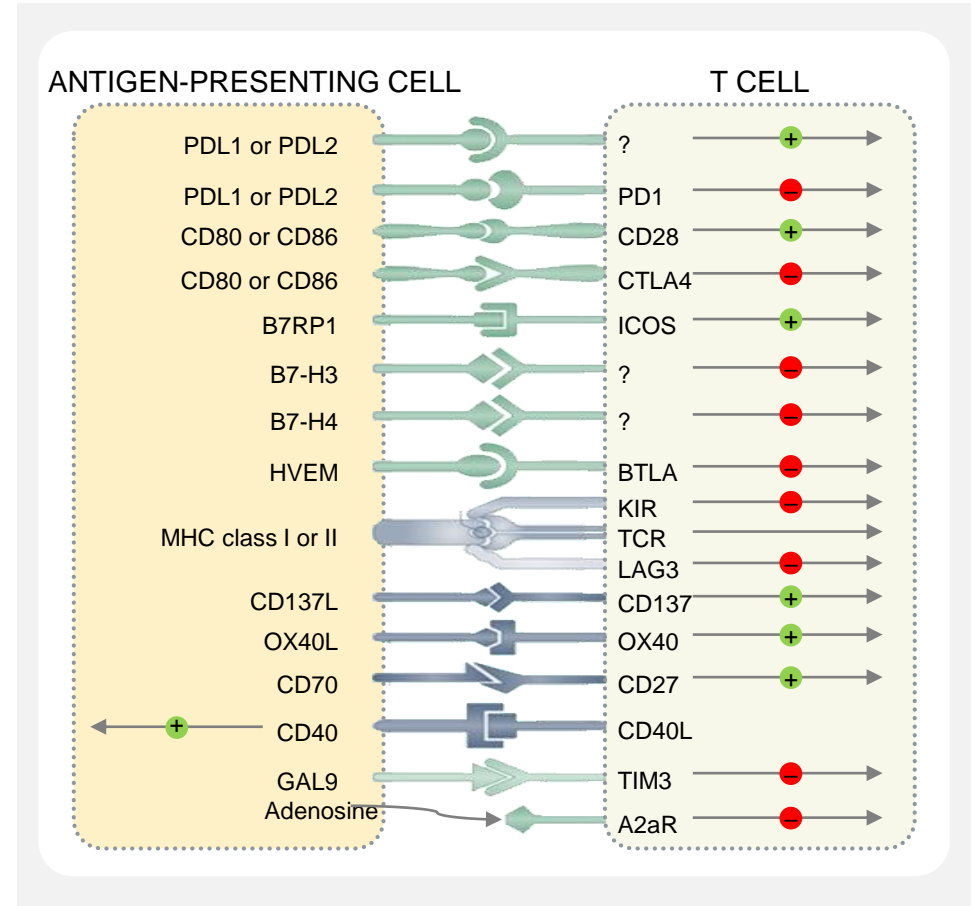


# ADC-1013: CD40 is a key immuno-oncology target

## ADC-1013 Mode of Action



## Immuno-modulating 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: One of four CD40 mAbs in clinical phase

## Selection of antibody based immuno-oncology drugs in clinical development

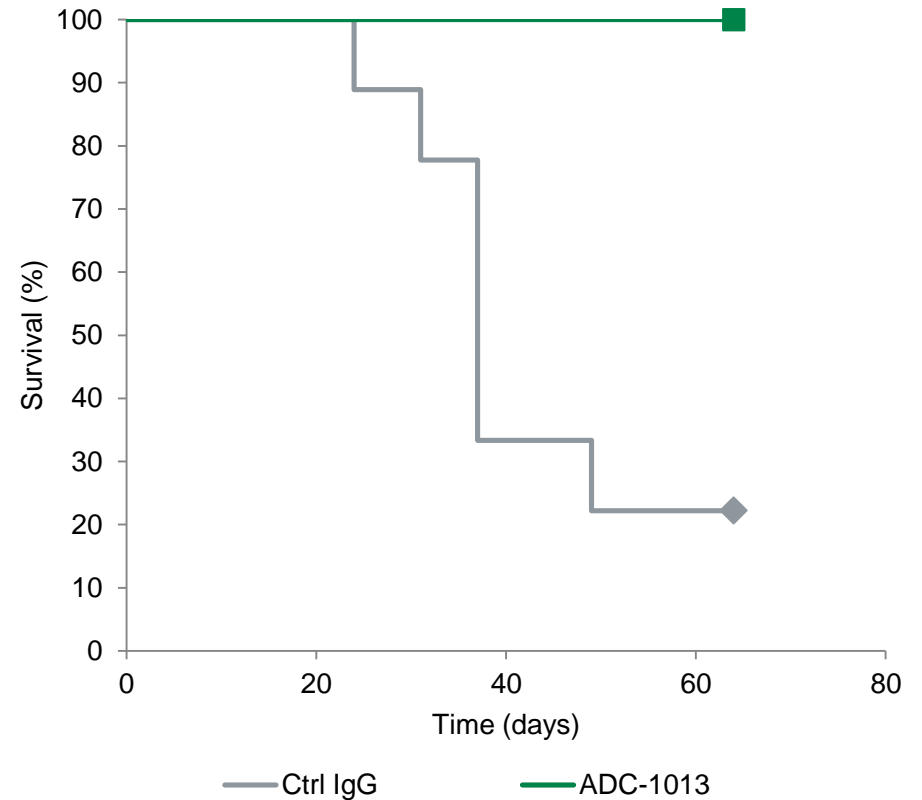
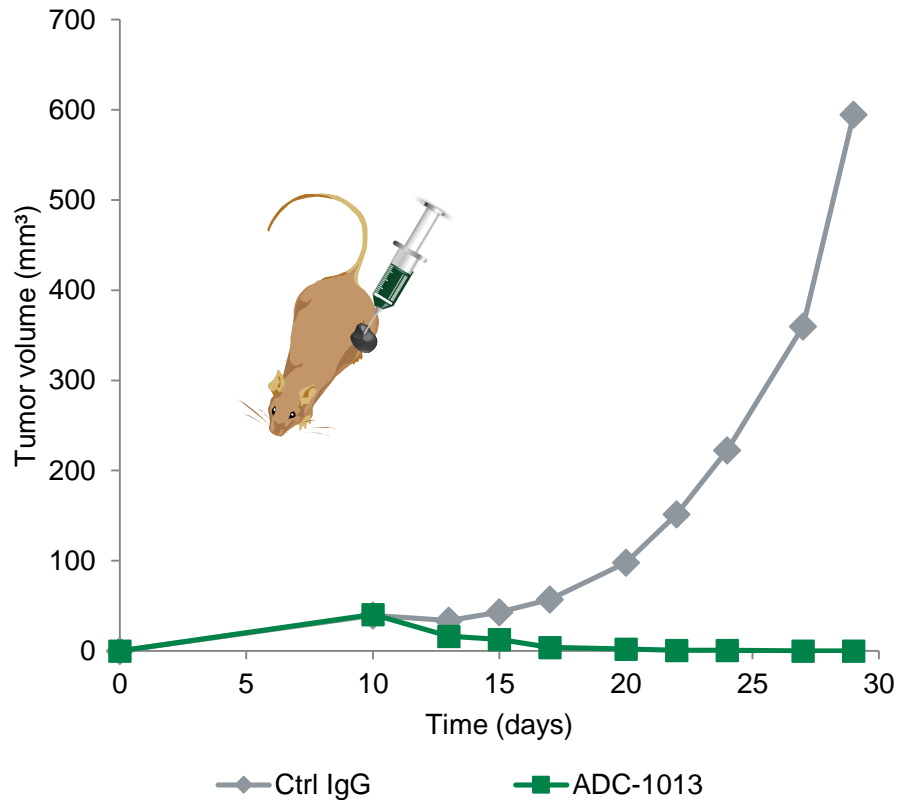
Company	Drug	Indication	Phase	Target
AstraZeneca (MedImmune)	durvalumab	NSCLC, H&N, bladder	III	PD-L1
Pfizer & AstraZeneca	tremelimumab	Mesothelioma, NSCLC, bladder	III	CTLA-4
Pfizer & MerckSerono	avelumab	NSCLC, GI, bladder	III	PD-L1
Prima Biomed (Immutep)	IMP-321	Breast	III	LAG3
AstraZeneca (MedImmune)	MEDI-0680	BCL, NHL, melanoma, CRC	II	PD-1
CureTech	pidilizumab	BCL, NHL, melanoma, CRC	II	PD-1
Jiangsu Hengrui Medicine (Incyte)	INCSHR-1210	Solid tumors	II	PD-1
Novartis	PDR-001	NSCLC, CRC, GI, melanoma	II	PD-1
Regeneron	REGN2810	Melanoma	II	PD-1
AgonOx (AstraZeneca)	MEDI-6469	Breast, prostate, lymphoma	II	OX40
Bristol-Myers Squibb	BMS-986178	Solid tumors	II	OX40
Bristol-Myers Squibb	urelumab	Solid tumors and lymphoma	II	CD137
Celldex	varlilumab	Solid tumors	II	CD27
Novartis	LAG-525	Solid tumors	II	LAG3
Novartis	MBG-453	Cancer	II	TIM-3
<b>Alligator Bioscience</b>	<b>ADC-1013</b>	<b>Solid tumors</b>	<b>I</b>	<b>CD40</b>
Apexigen	APX-005M	Lymphoma	I	CD40
Roche	RG-7876	Solid tumors	I	CD40
Seattle Genetics	SEA-CD40	Solid tumors	I	CD40
Bristol-Myers Squibb	BMS-986016	Solid tumors, lymphoma and leukemia	I	LAG3
Merck	MK-4280	Cancer	I	LAG3
Novartis (Immutep)	IMP-701	Cancer	I	LAG3
Pfizer	PFE-1, PF-05082566	Solid tumors and lymphoma	I	CD137
Agenus and Incyte	INCAGN1876	Solid tumors	I	GITR
Amgen	AMG-228	Solid tumors	I	GITR
AstraZeneca	MEDI-1873	Solid tumors	I	GITR
Bristol-Myers Squibb	BMS-986156	Solid tumors	I	GITR
GITR Inc	TRX-518	Solid tumors and melanoma	I	GITR
Merck	MK-4166	Solid tumors	I	GITR
Merck	MK-1248	Cancer	I	GITR
Novartis	GWN-223	Solid tumors and lymphoma	I	GITR
AstraZeneca	MEDI-0562	Cancer	I	OX40
GlaxoSmithKline	GSK-3174998	Cancer	I	OX40
Pfizer	PF-04518600	Cancer	I	OX40
Roche	RG7888	Solid tumors	I	OX40
Merck	M-7824	Solid tumors	I	PD-L1 and TGF- $\beta$
Bristol-Myers Squibb	MDX-1105	Solid tumors	I	PD-L1
BeiGene	BGB-A317	Cancer	I	PD-1
GlaxoSmithKline (Amplimmune)	AMP-224	Cancer	I	PD-1
Regeneron	REGN-2810	Solid tumors, BCL	I	PD-1
Daiichi Sankyo	DS-5573	Solid tumors	I	B7-H3
MacroGenics	Enoblituzumab	Solid tumors	I	B7-H3
GlaxoSmithKline	GSK-3359609	Cancer	I	ICOS
Jounce Therapeutics	JTX-2011	Cancer	I	ICOS
Tesaro / Anaptys	TSR-022	Cancer	I	TIM-3

## Comments

- Approx. 70 immuno-oncology drugs are currently in clinical development
- Extensive focus on first generation targets PD-1 and PD-L1
- Four ongoing trials of by commercial companies targeting the CD40 receptor with monospecific agonistic antibodies, including Alligator's ADC-1013

# ADC-1013: Anti-tumor effect in lymphoma model

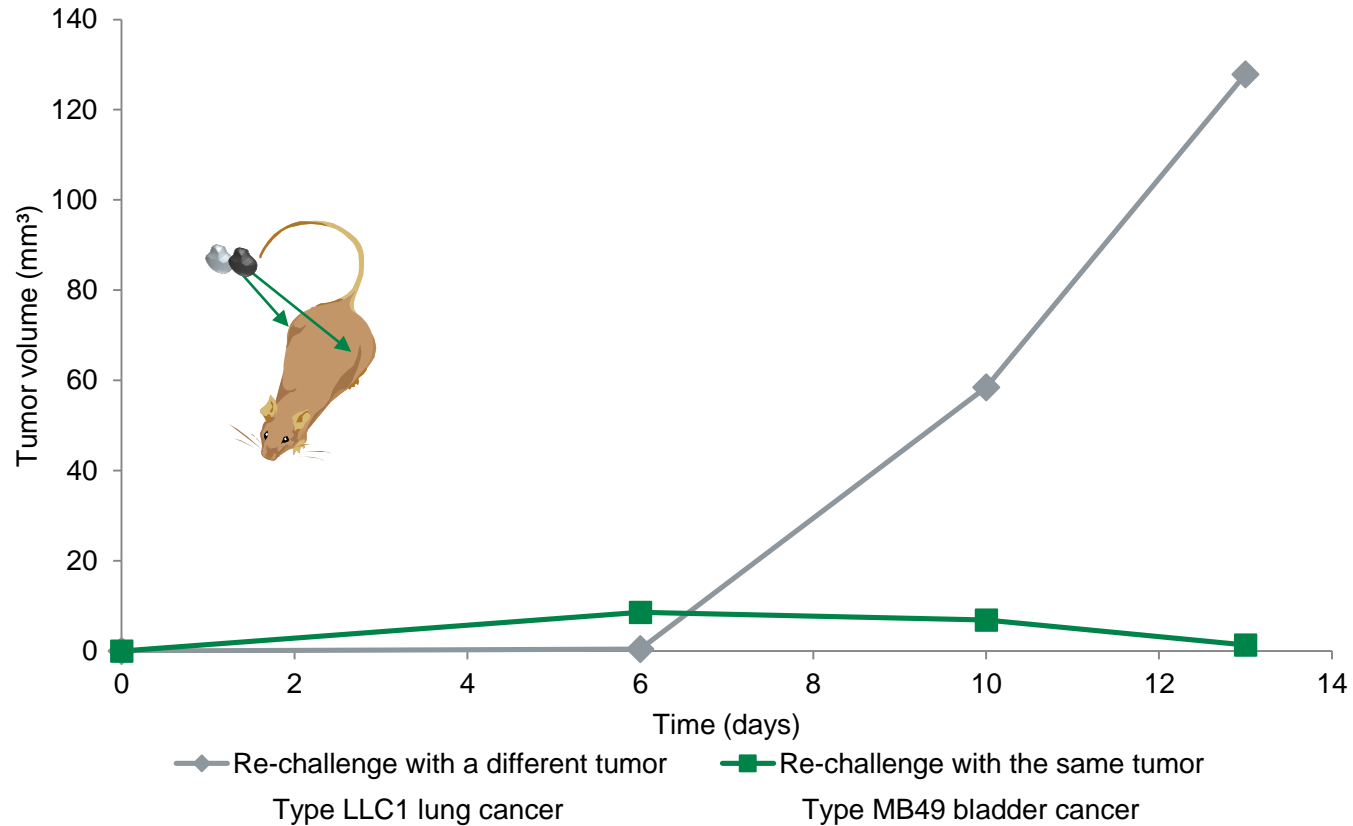
Results from single tumor model in A20 lymphoma



ADC-1013 induces significant anti-tumor effects in a hCD40 negative lymphoma model (A20)

# ADC-1013: Long term immunity in bladder model

Results from rechallenge in a twin-tumor model



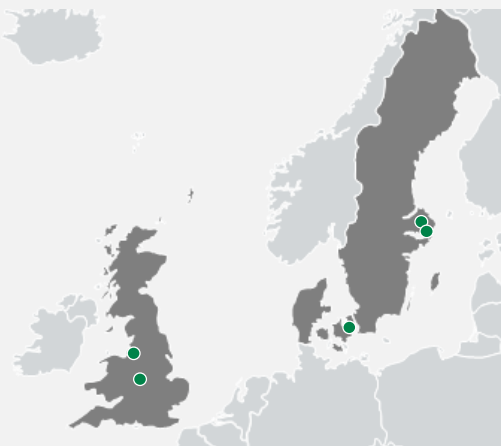

Mice previously treated with ADC-1013 exhibit tumor immunity to identified tumor type

# ADC-1013: Partnership with Janssen validating Alligator's model

## Partnership details for ADC-1013

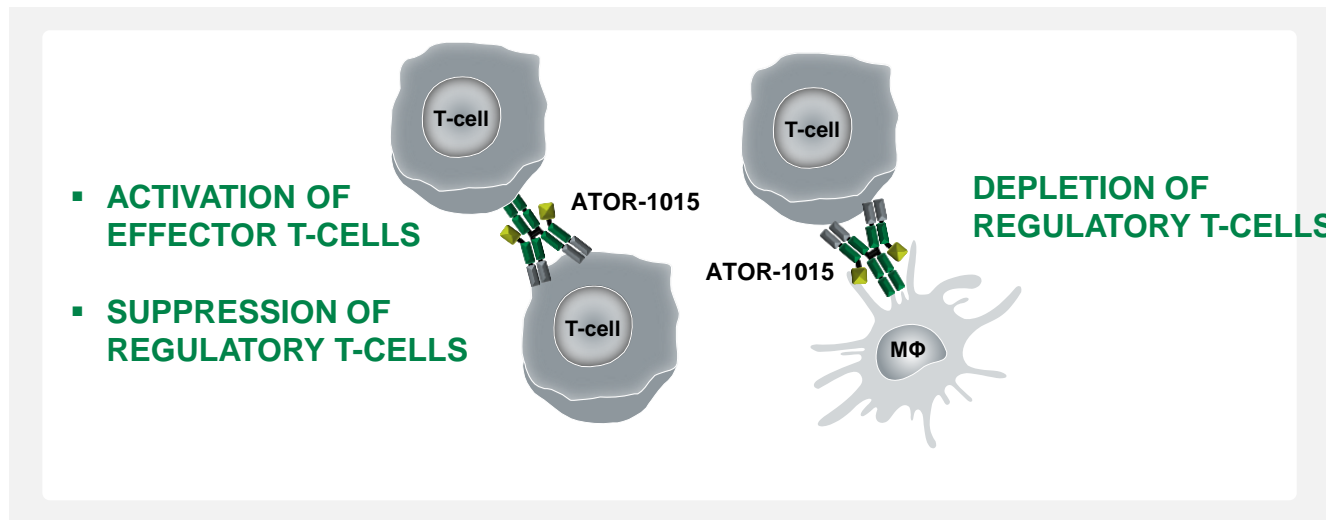
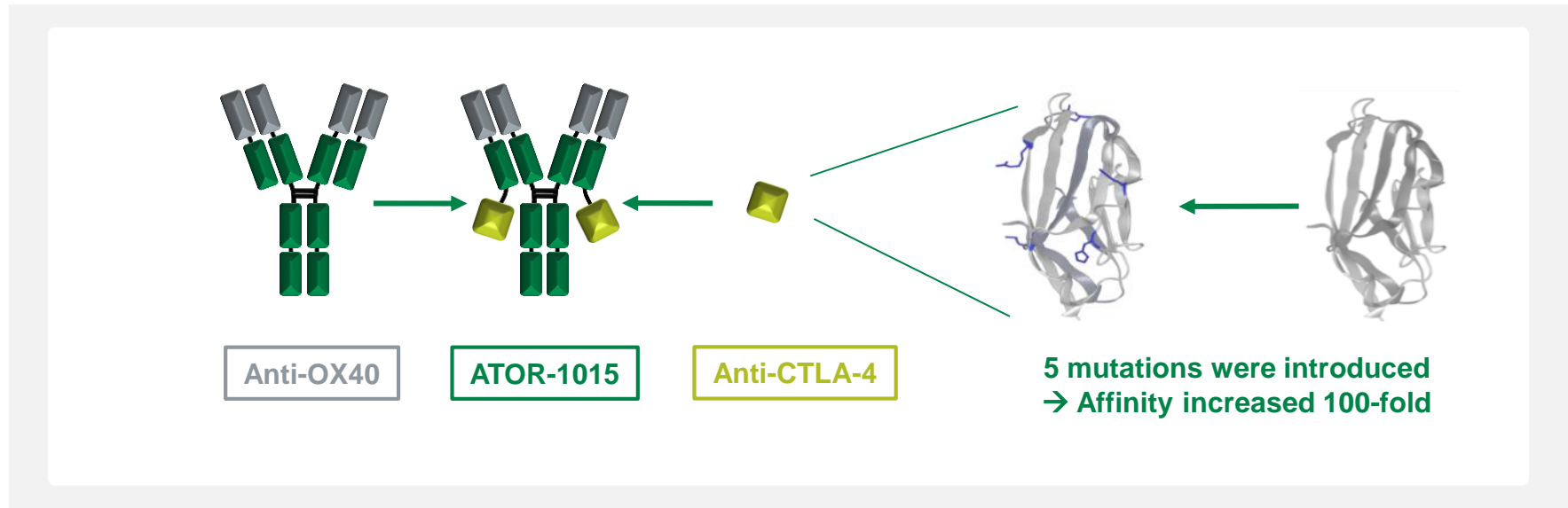
Description of agreement	Royalty / Milestone potential
<ul style="list-style-type: none"> <li>▪ Exclusive world-wide license to ADC-1013</li> <li>▪ Alligator sponsor for the ongoing Phase I clinical trial</li> <li>▪ Additional phase I study initiated by Janssen</li> <li>▪ All development costs covered by Janssen</li> </ul>	<ul style="list-style-type: none"> <li>▪ Up-front payment plus additional milestones up to a potential total of US\$695 million</li> <li>▪ Tiered high single-digit to low double digit royalties on worldwide net sales upon successful launch</li> </ul>

## Description of ongoing Phase I trial

			<p>→ 40 patients with advanced solid tumors</p> <p>→ 5 clinical sites in the UK, DK and SE</p> 
Dosing & administration	Primary endpoint	Secondary endpoints	
<ul style="list-style-type: none"> <li>▪ FiH, first dose April 2015</li> <li>▪ Dose escalation</li> </ul>	<ul style="list-style-type: none"> <li>▪ Safety and tolerability</li> </ul>	<ul style="list-style-type: none"> <li>▪ Pharmacokinetics</li> <li>▪ Immunogenicity</li> <li>▪ Clinical efficacy</li> </ul>	

Highly attractive out-licensing terms with Janssen showing commitment through extension of clinical scope to systemic administration

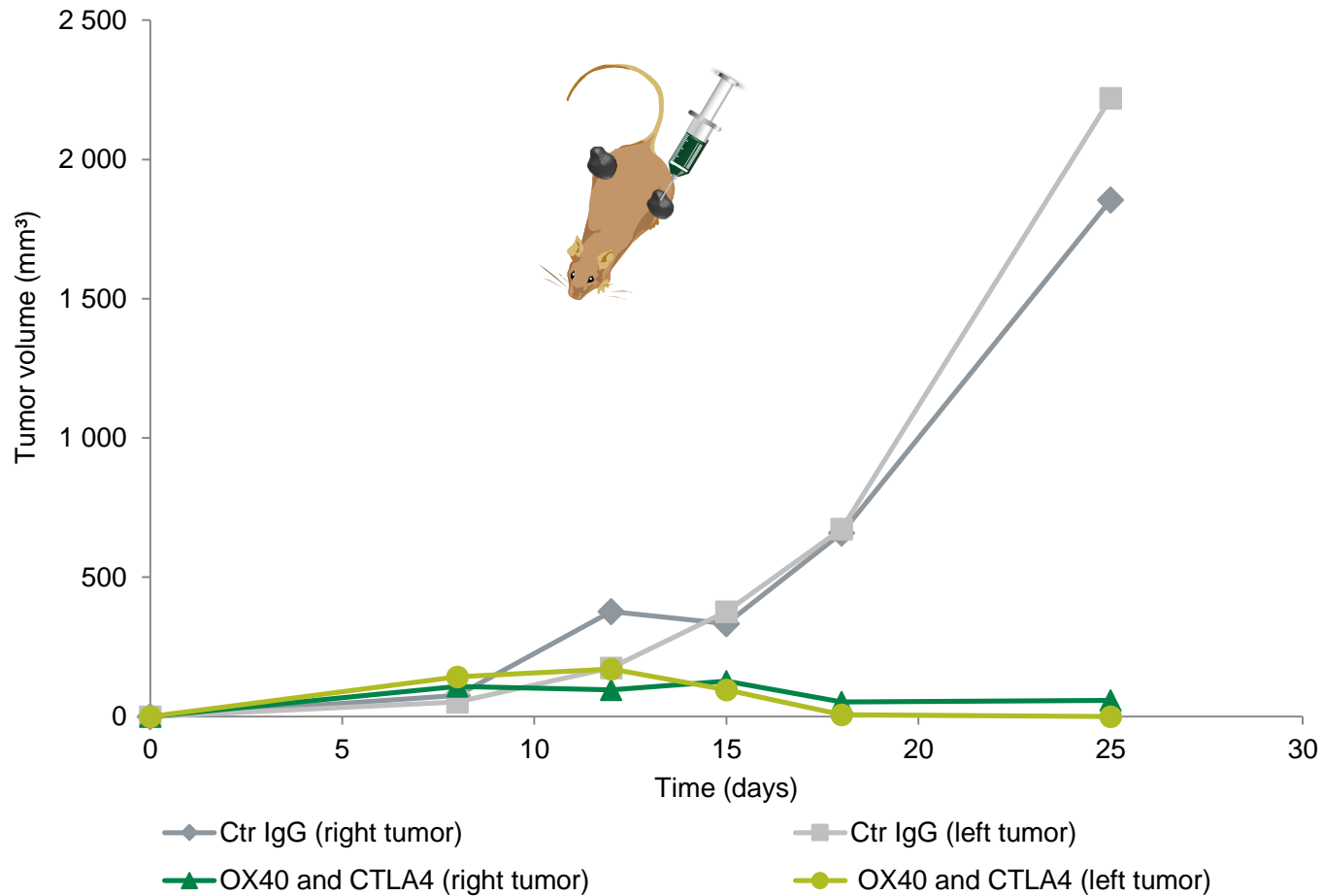
# ATOR-1015: Biological rationale for dual binding OX40 and CTLA-4





# ATOR-1015: Combining OX40 with CTLA-4 (1/3)

OX40 and CTLA-4 surrogate antibodies (30 $\mu$ g of each)

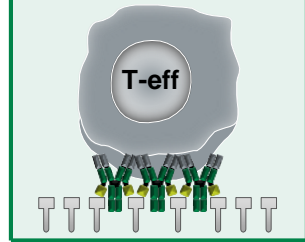


# ATOR-1015: Combining OX40 with CTLA-4 (2/3)

## CTLA-4 mediated clustering of OX40

### CTLA-4 mediated clustering

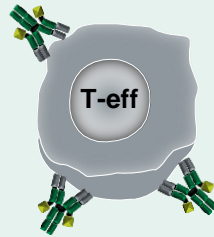
- Strong immune activation



CTLA-4 coated wells

### No clustering

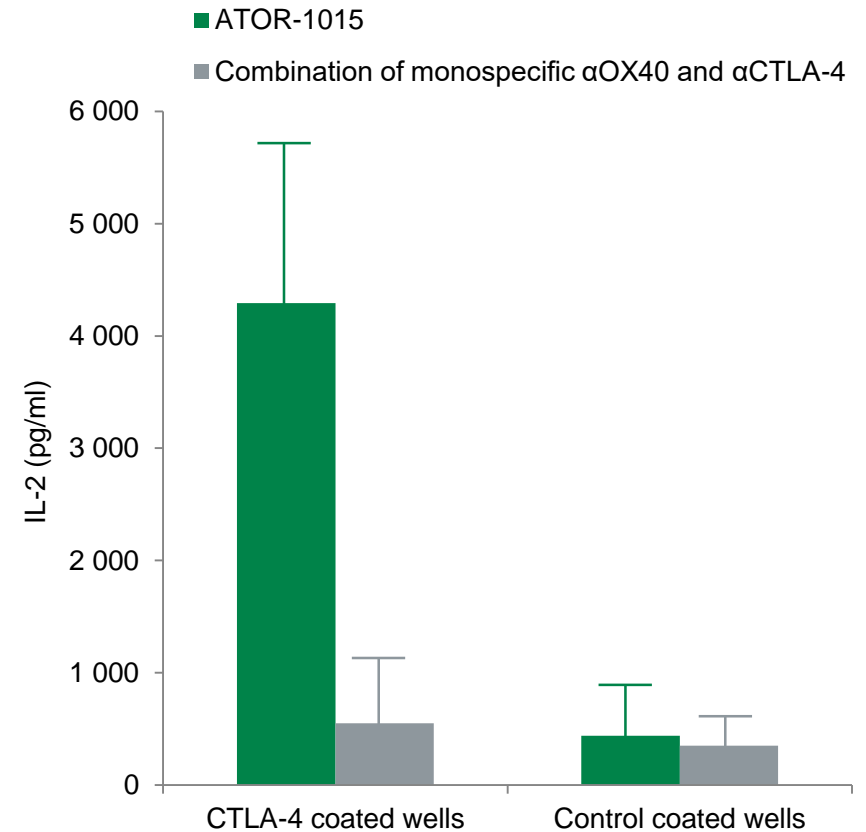
- No/low immune activation



Control coated wells

- When ATOR-1015 binds to CTLA-4 coated on the surface of a well it induces extensive cross-linking of OX40 on the T-cells resulting in a very strong immune activation
- The activation is superior to the combination of the monospecific  $\alpha$ OX40 and  $\alpha$ CTLA-4 binders

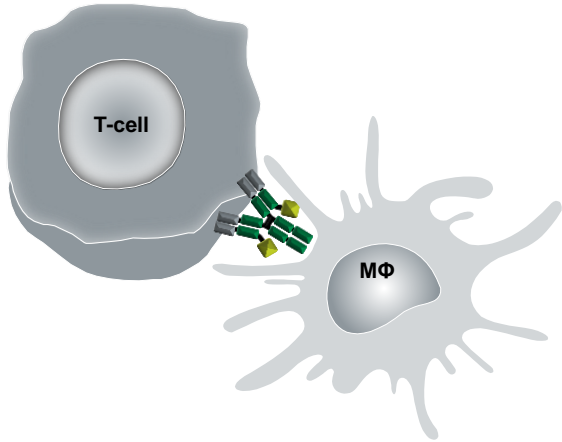
## Synergistic T-eff activation



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

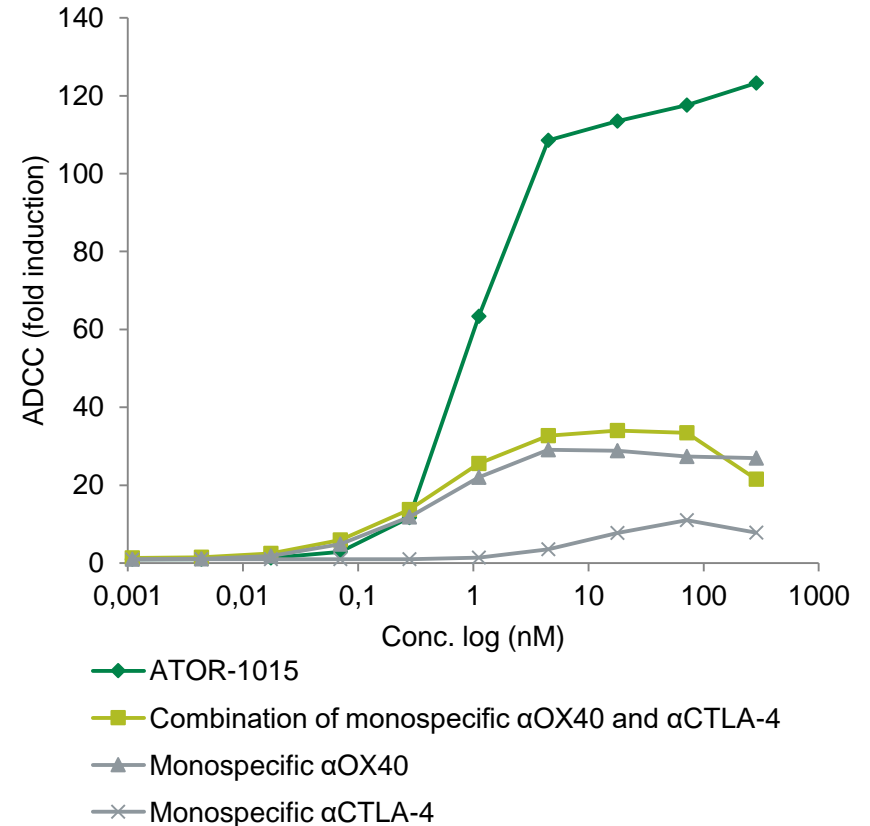
# ATOR-1015: Combining OX40 with CTLA-4 (3/3)

ATOR-1015 induces ADCC on CTLA-4/OX40 expressing cells



- When ATOR-1015 binds to cells that express high levels of OX40 and CTLA-4 (e.g. regulatory T-cells) it can induce ADCC
- The ability to induce ADCC is superior to the combination of the monospecific  $\alpha$ OX40 and  $\alpha$ CTLA-4 binders

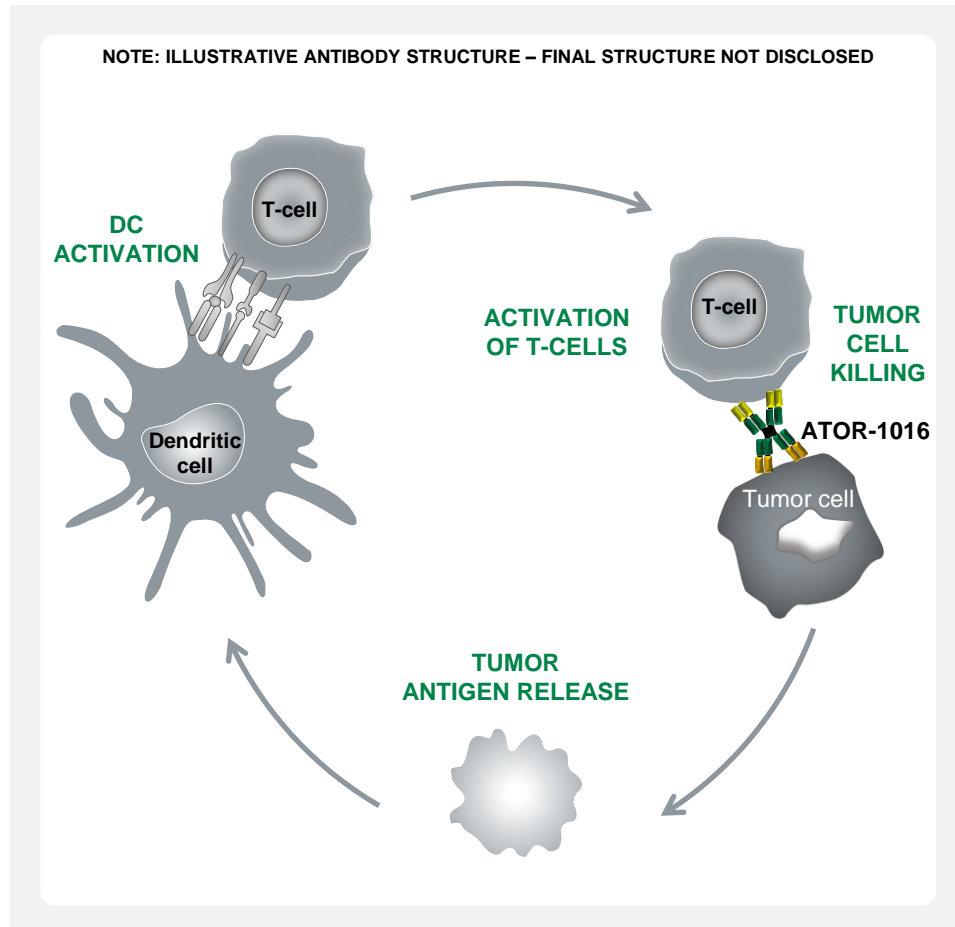
Synergistic T-cell depletion



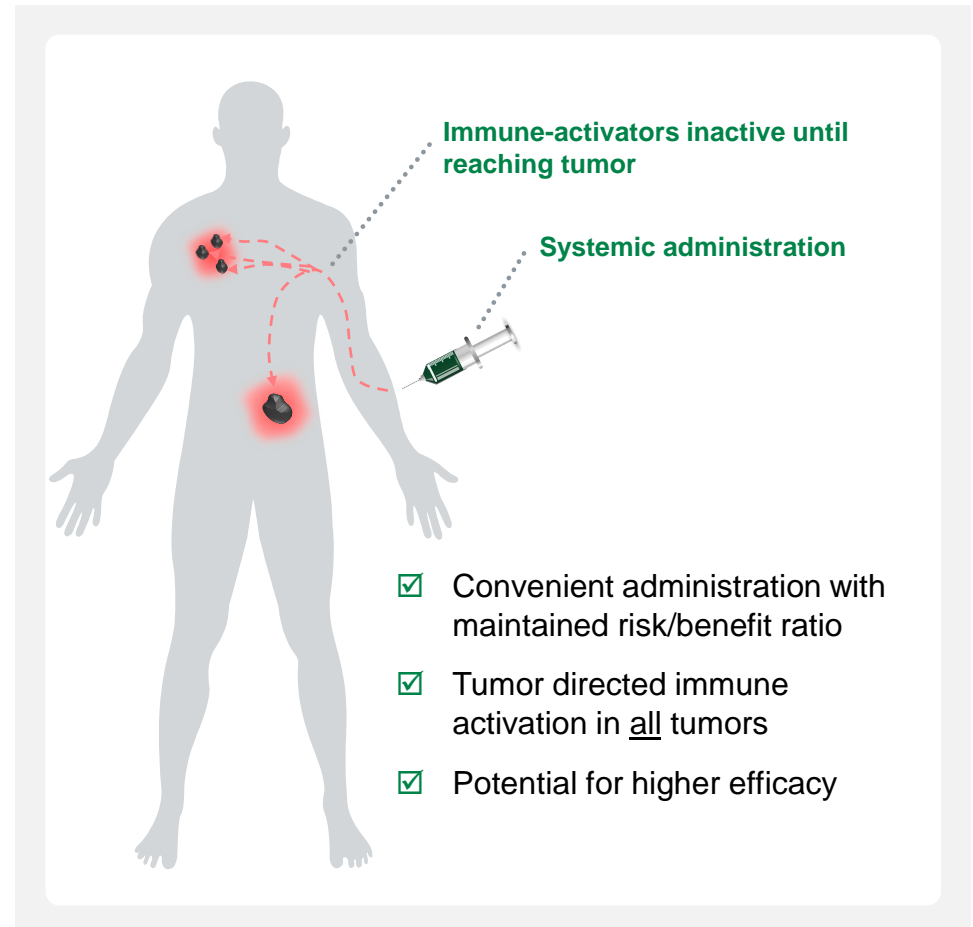
The effect of the bispecific antibody is superior to the effect of the combination of the monospecific antibodies

# ATOR-1016: Localizing tumor-directed immunotherapy

## Mode of Action



## Major benefits of localizing immune-activators



Localizing tumor-directed immunotherapy has substantial potential in cancers with multiple metastases

# Solid intellectual property portfolio

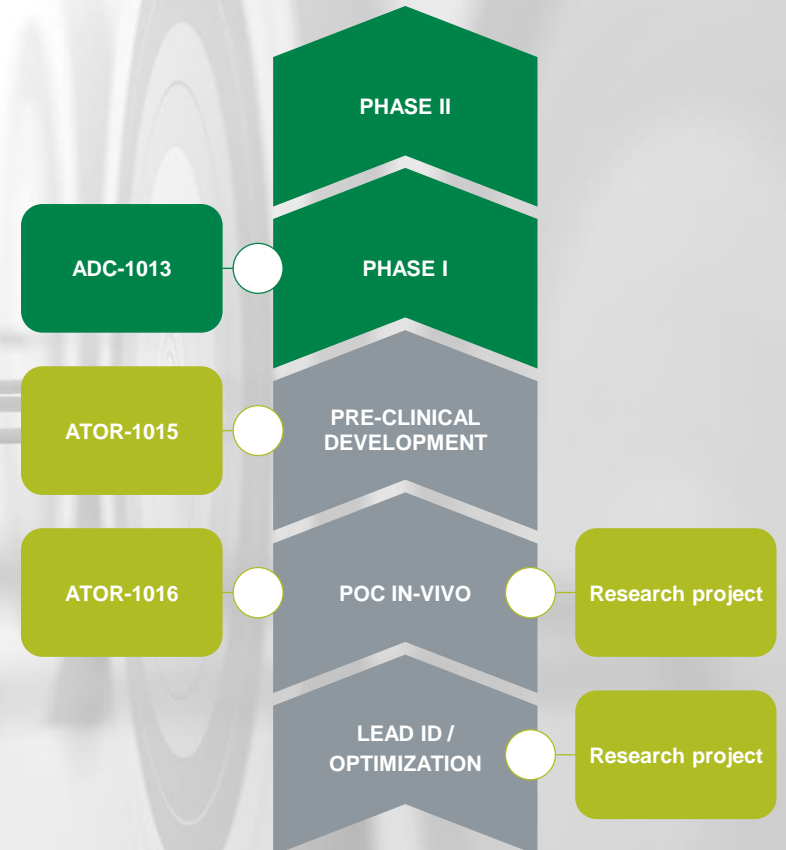
- More than 50 approved and/or pending patents
- Seven product patent families, including ADC-1013
- Solid IP position for ADC-1013 with patent coverage at least until 2032
- Four technology patent families, including FIND® and ALLIGATOR-GOLD®
- Covering all major markets (US, EU, Japan, BRIC)

Source: Company information



# Strategy to maximize shareholder value

1. **Advance and broaden pipeline** of agonistic tumor-directed immuno-oncology antibodies
2. **Extend in-house product development** to later-stage clinical phase prior to partnering
3. **Development of next generation technology** for antibody discovery and optimization
4. **Facilitate an attractive research environment** for intellectual human capital







**Thank You**