



# Immuno-Oncology

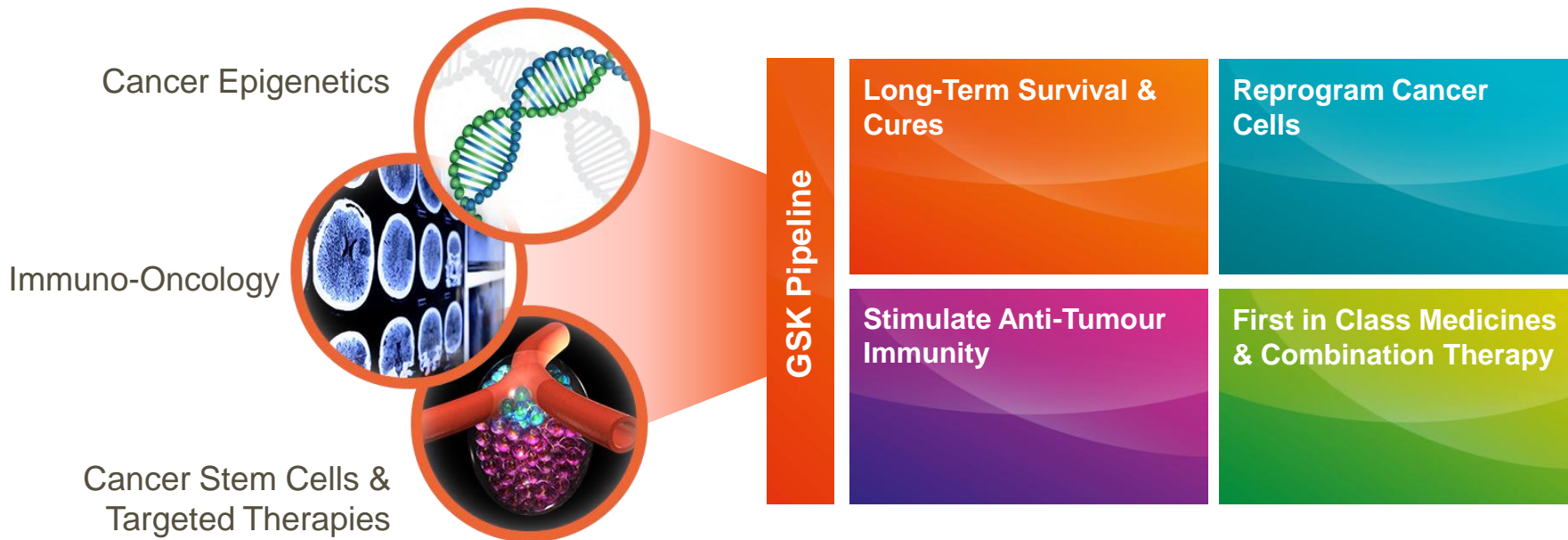
*Axel Hoos, MD, PhD*

*Senior Vice President, Oncology R&D*

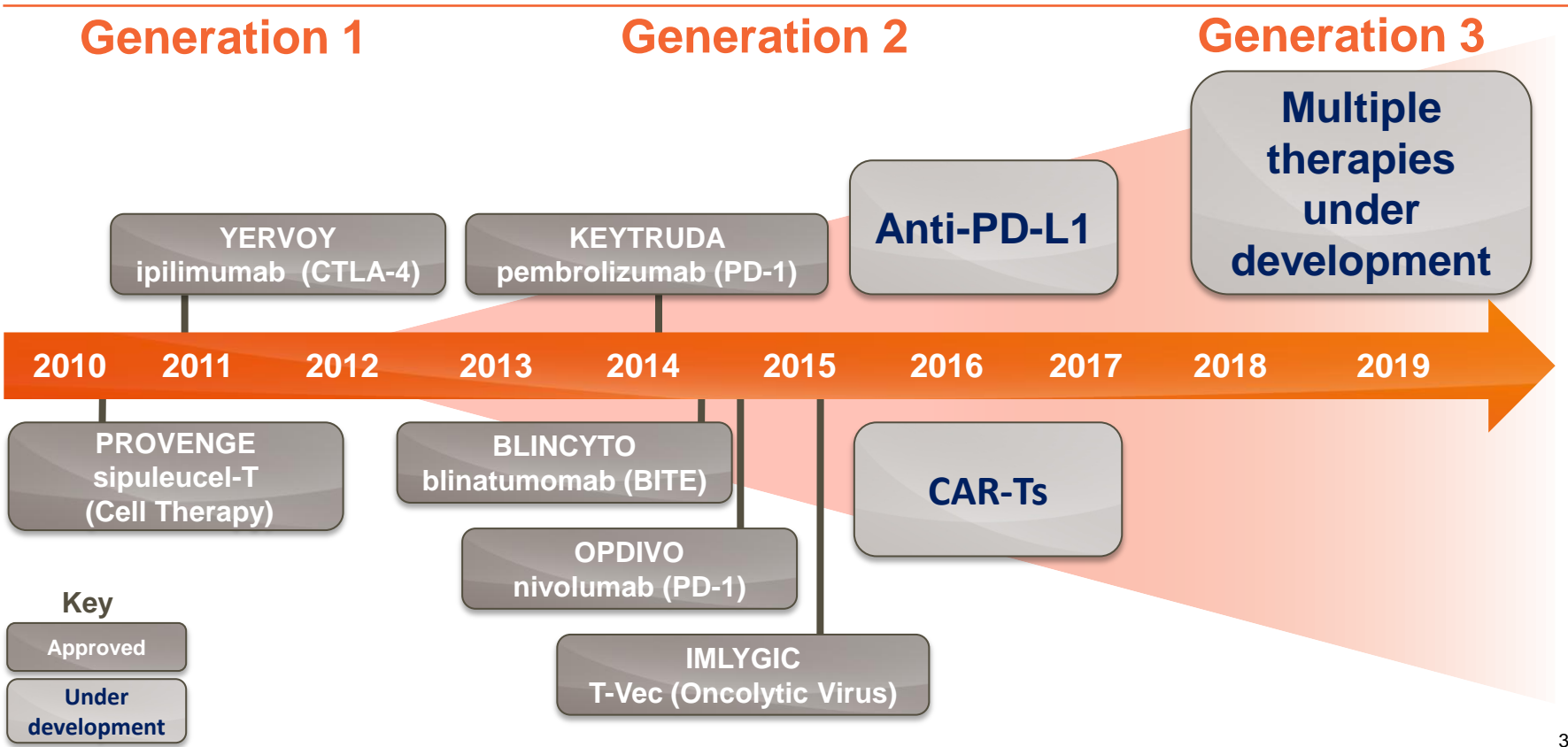
February 24, 2016

# Oncology R&D strategy

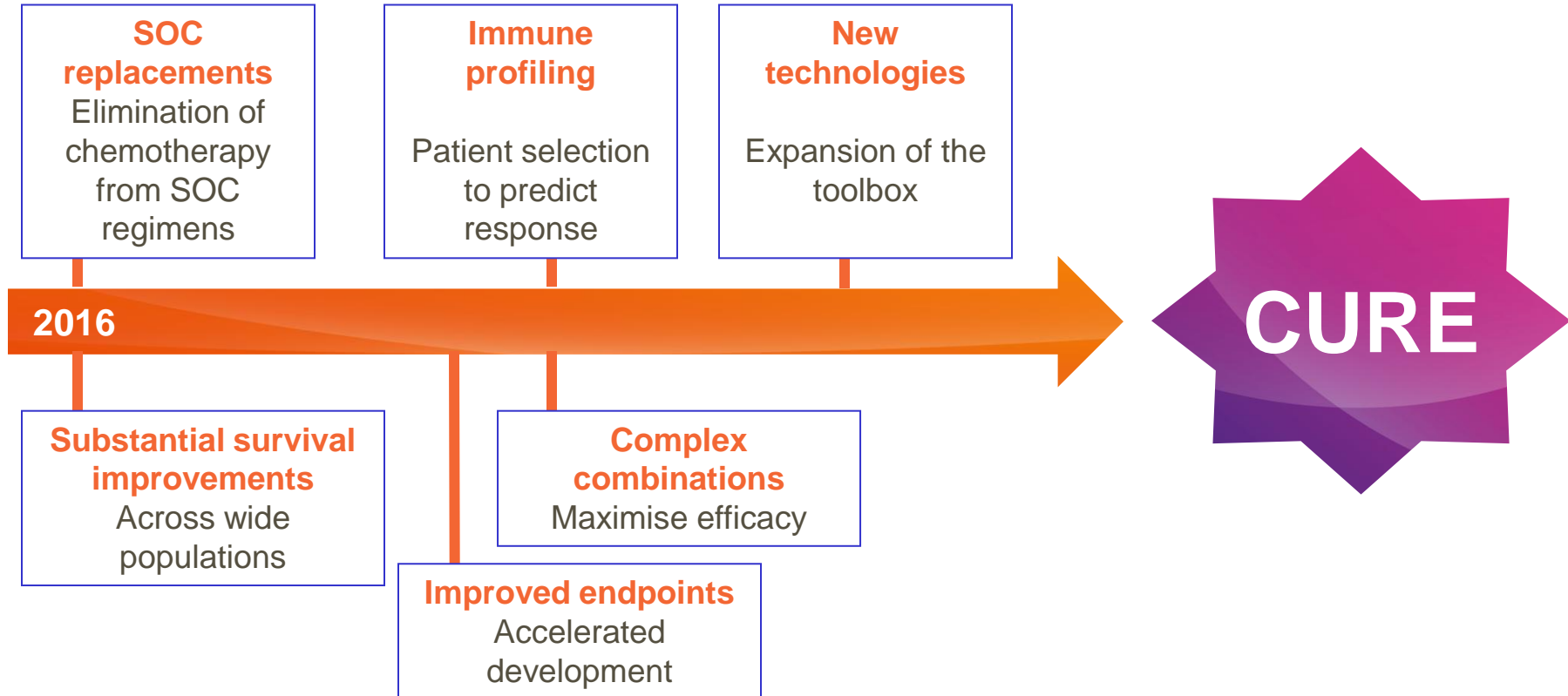
*Focusing on 3 areas fundamental to oncology*



# 3 Generations of therapies

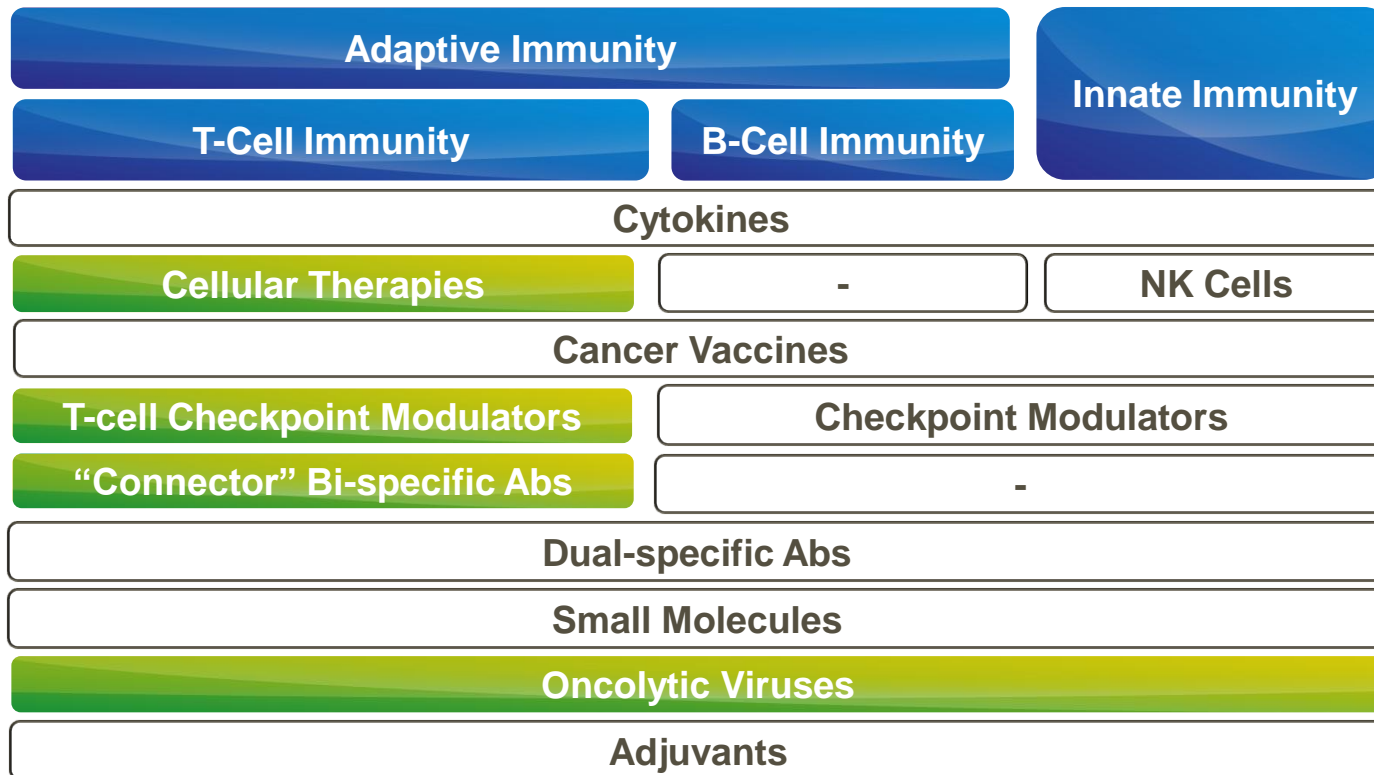


# Main trends



# 3<sup>rd</sup> Generation opportunities

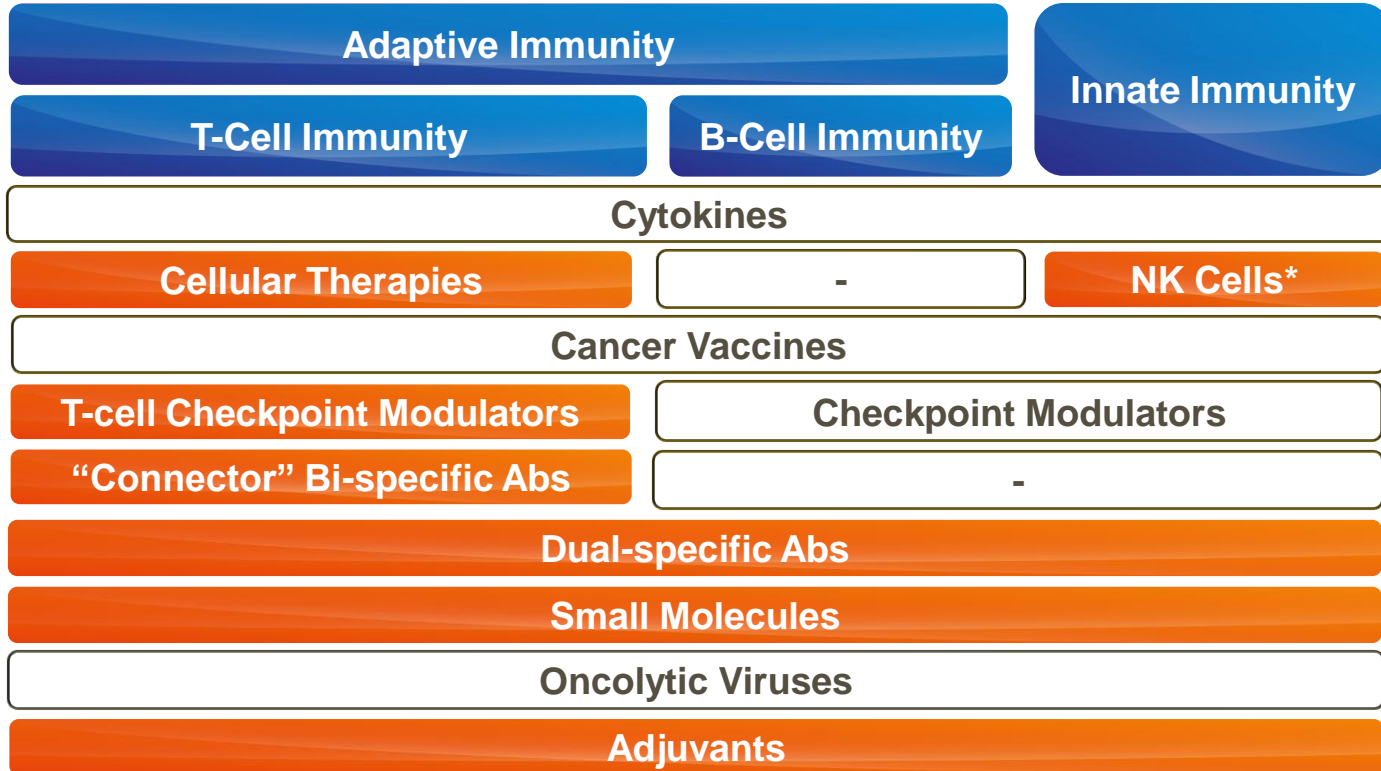
*Spectrum of immuno-oncology modalities*



 Approved therapies

# 3<sup>rd</sup> Generation opportunities

GSK's multi-modality pipeline



# 3<sup>rd</sup> Generation leadership



*Innovation across novel targets, modalities and combinations (5 in the clinic)*

Modality	Program	Mechanism	Pre-clinical	Phase 1	Phase 2
mAbs	GSK3174998	OX40 agonist	Solid Tumours, Heme Malignancies		
	GSK3359609	ICOS agonist			
	GSK2857916	BCMA -ADC	Multiple Myeloma		
	Brontictuzumab *	Notch1	Solid Tumours, Heme Malignancies		
	Tarextumumab *	Notch2/3	SCLC		
	GSK	Immune checkpoints			
Cell Therapy	NY-ESO-1*	TCR-T	Sarcoma, Multiple Myeloma, NSCLC, Ovarian, Melanoma		
	GSK/Adaptimmune	TCR-T			
	GSK	CAR-T			
Synthetic / Small Molecules	GSK1795091	TLR-4 agonist			
	GSK	Novel mechanisms			
Bi-Specific Molecules	GSK/ImmunoCore	ImmTacs			
	GSK	mAb-dAbs			
	GSK/AdiMab	Dual-specific Abs			

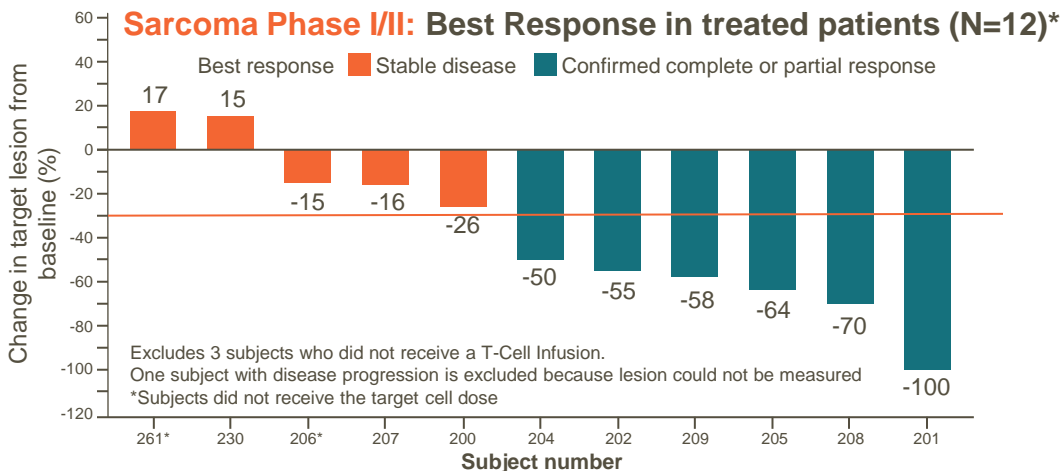
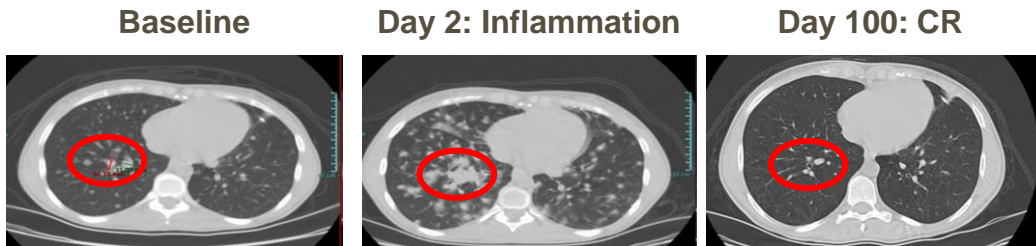
\* Collaboration with third party

# NY-ESO T-Cell Therapy



- TCR T-cell therapy
- 50% ORR seen in sarcoma
- Ongoing studies in ovarian and other solid tumours and haematological malignancies
- Planned studies in combination with checkpoint modulators
- Collaboration with Adaptimmune

## Sarcoma Phase I/II: Individual patient complete response (CR)



Status: Phase I/II  
 Indications: NY-ESO-1 positive Cancers:  
 Sarcoma, Myeloma, NSCLC,  
 Melanoma, Ovarian Cancer  
 Filing strategy to be agreed with Adaptimmune

Note: GSK3377794 subject to exercise of option by GSK

GSK, data on file.



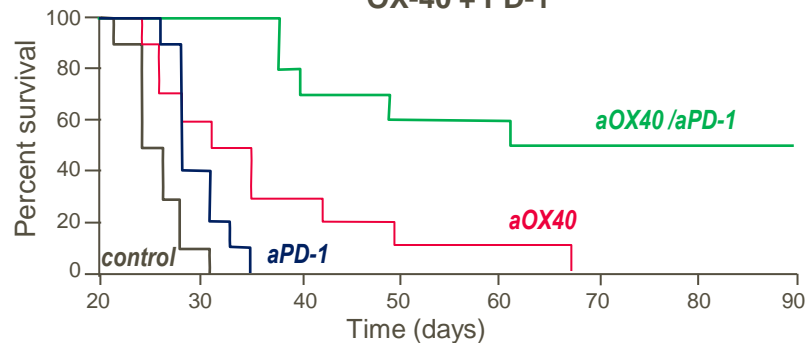
# GSK3174998 OX40 agonist mAb



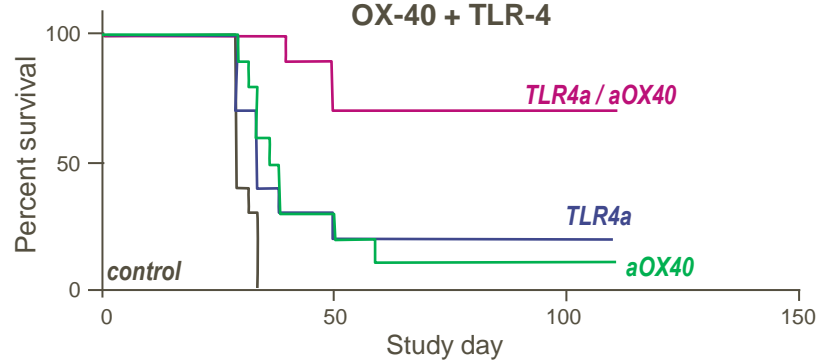
- GSK3174998 is one of four humanised OX-40s in clinic
- Dual mechanism: enhancing effector T-cell and suppressing T-regs
- Phase I Study started in eight cancers
- Combination with Merck PD1 in 2016
- Combination with GSK TLR4 in 2017
- Collaboration with MD Anderson

Status: Phase I  
Indications: Solid tumours, Heme Malignancies  
Planned Filing: 2020

Survival in animal model (CT26)  
OX-40 + PD-1



Survival in animal model (CT26)  
OX-40 + TLR-4



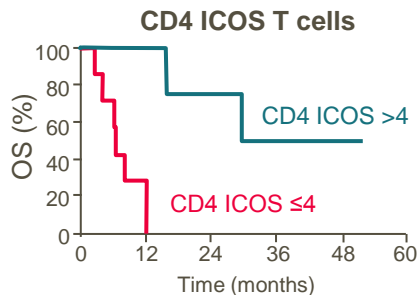
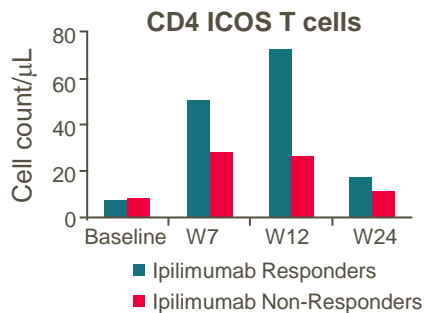
# GSK3359609 first-in-class ICOS agonist antibody



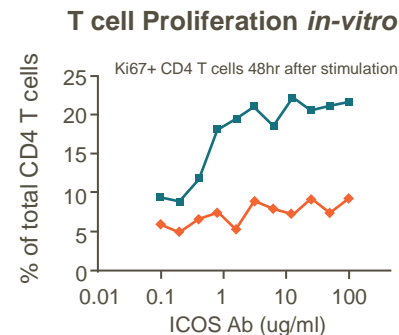
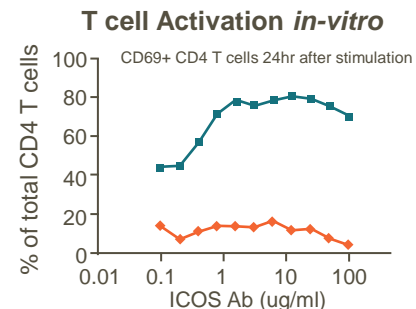
- Universal mechanism across multiple cancers
- Patient selection biomarker
- Enhances T-cells associated with survival
- Use after CTLA-4 and PD-1 in unresponsive or refractory patients
- Possible anchor for use in combinations
- Collaboration with INSERM

Status: Phase I start Q1 2016  
Indications: Solid tumours, Heme Malignancies  
Planned Filing: 2020

## ICOS in ipilimumab-treated patients



## GSK3359609

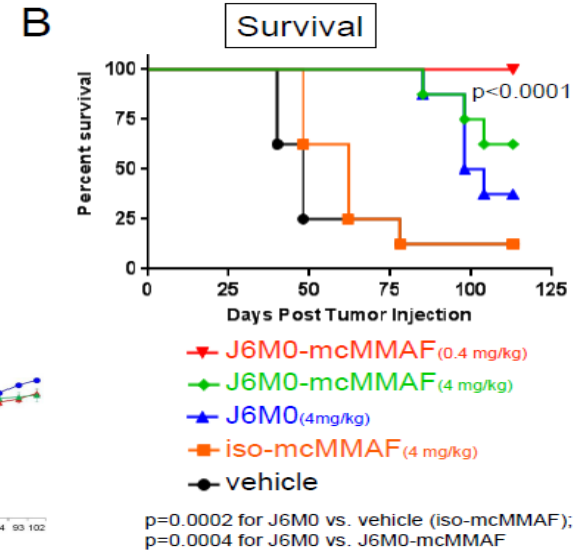
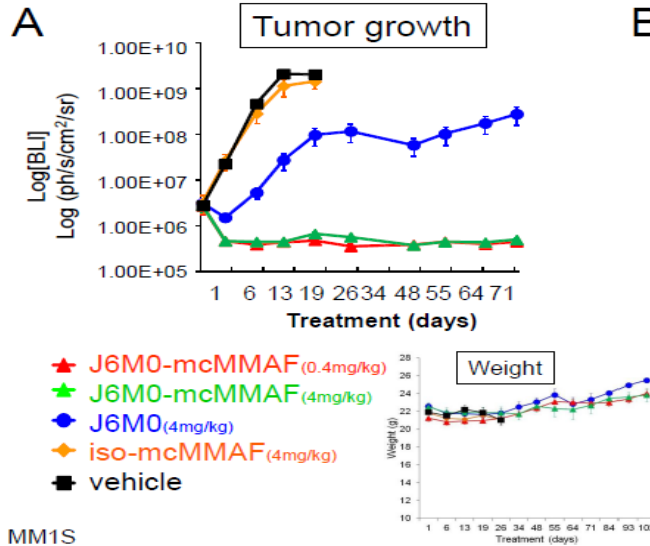


# GSK2857916 BCMA-ADC



- B Cell Maturation Antigen
- Antibody Drug Conjugate (ADC) with MMAF (auristatin derivative)
- High-expression target in multiple myeloma
- ADCC enhanced
- Immunogenic cell death inducer
- Strong pre-clinical activity
- High potential for combinations

## Bone Marrow Dissemination Model (SCID Mice)



Status: Phase I  
 Indications: Multiple Myeloma  
 Planned Filing: Data dependent (post 2020)

Tai et al, Blood (2014), 123(20):3128-38

# Immuno-Oncology at GSK



*Mission: Maximise patient survival*

*Achieve a long-term leadership position in Oncology*

## Scientific Focus

- **Optimise T-cell Immunity**  
Rationale: has delivered transformational medicines
- **Synergies and transformational effects through combinations**

## Tactics

- **Diversified pipeline**
  - Across key modalities
- **Innovation**
  - 3<sup>rd</sup> generation targets, modalities & combinations
- **Build world-class discovery and development team**
- **Fully-integrated programs** from early discovery through licensure
- **Partnerships**
  - Best science
  - Access to combinations

## Goals

- **Transformational effects for patients**
  - Maximise survival
- **Pipeline sustainability**
- **Long-term leadership position in Oncology**