GSK Oncology

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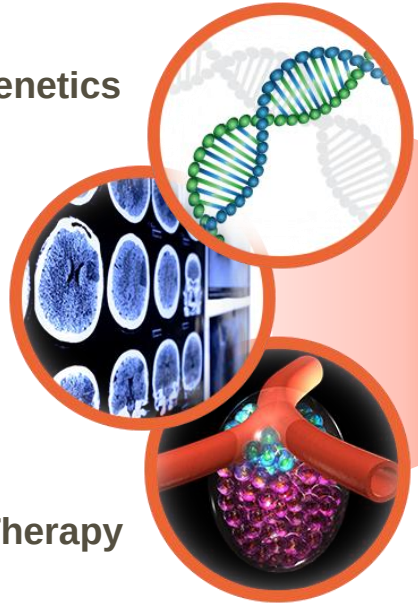
Oncology R&D Strategy

Maximizing survival through transformational medicines and combinations

Cancer Epigenetics

Immuno-Oncology

Cell & Gene Therapy



GSK pipeline

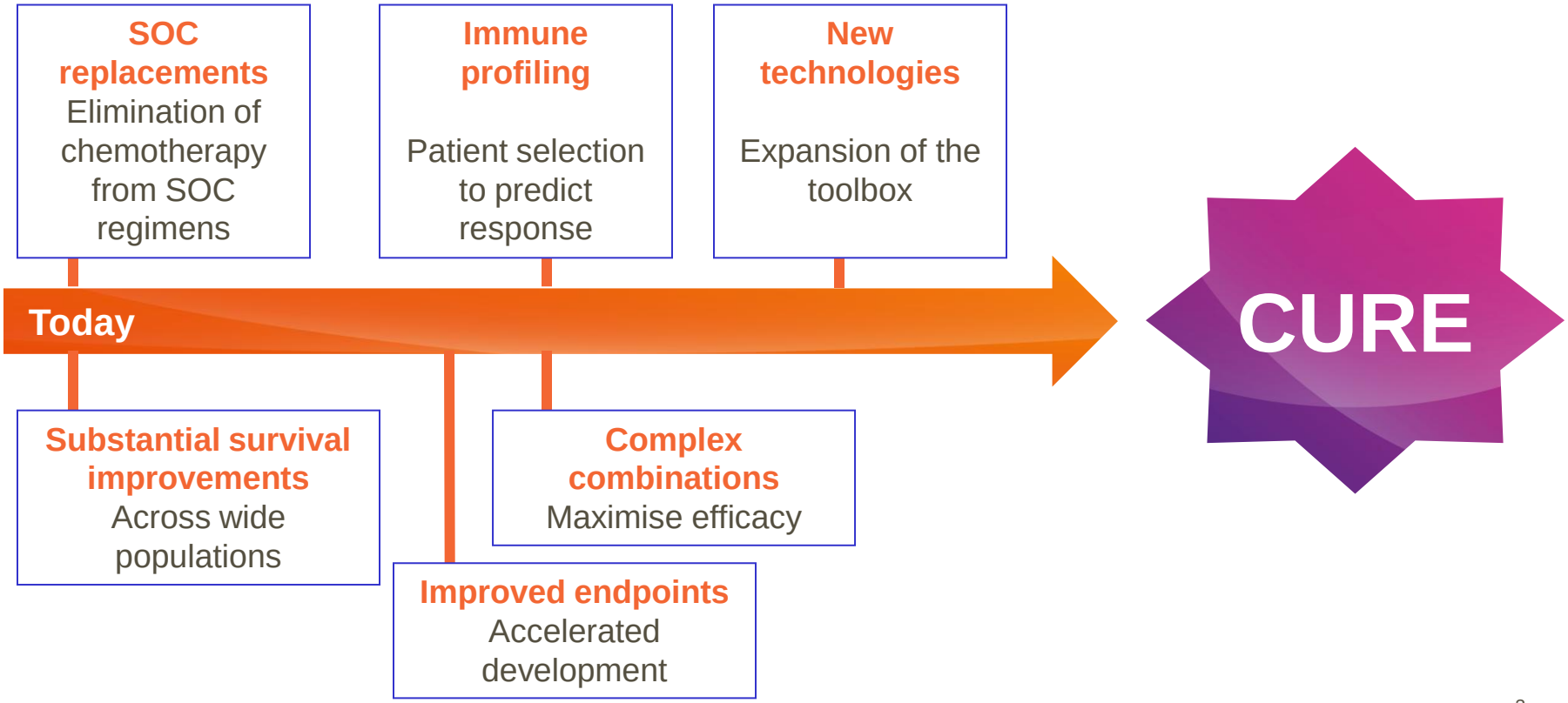
Long-term survival & cures

Reprogram cancer cells
Stimulate anti-tumour immunity
Cells as medicines

First-in-class medicines

Combination therapy

Main Trends


SOC replacements
Elimination of chemotherapy from SOC regimens
Immune profiling
Patient selection to predict response
New technologies
Expansion of the toolbox
Today
CURE
Substantial survival improvements
Across wide populations
Improved endpoints
Accelerated development
Complex combinations
Maximise efficacy

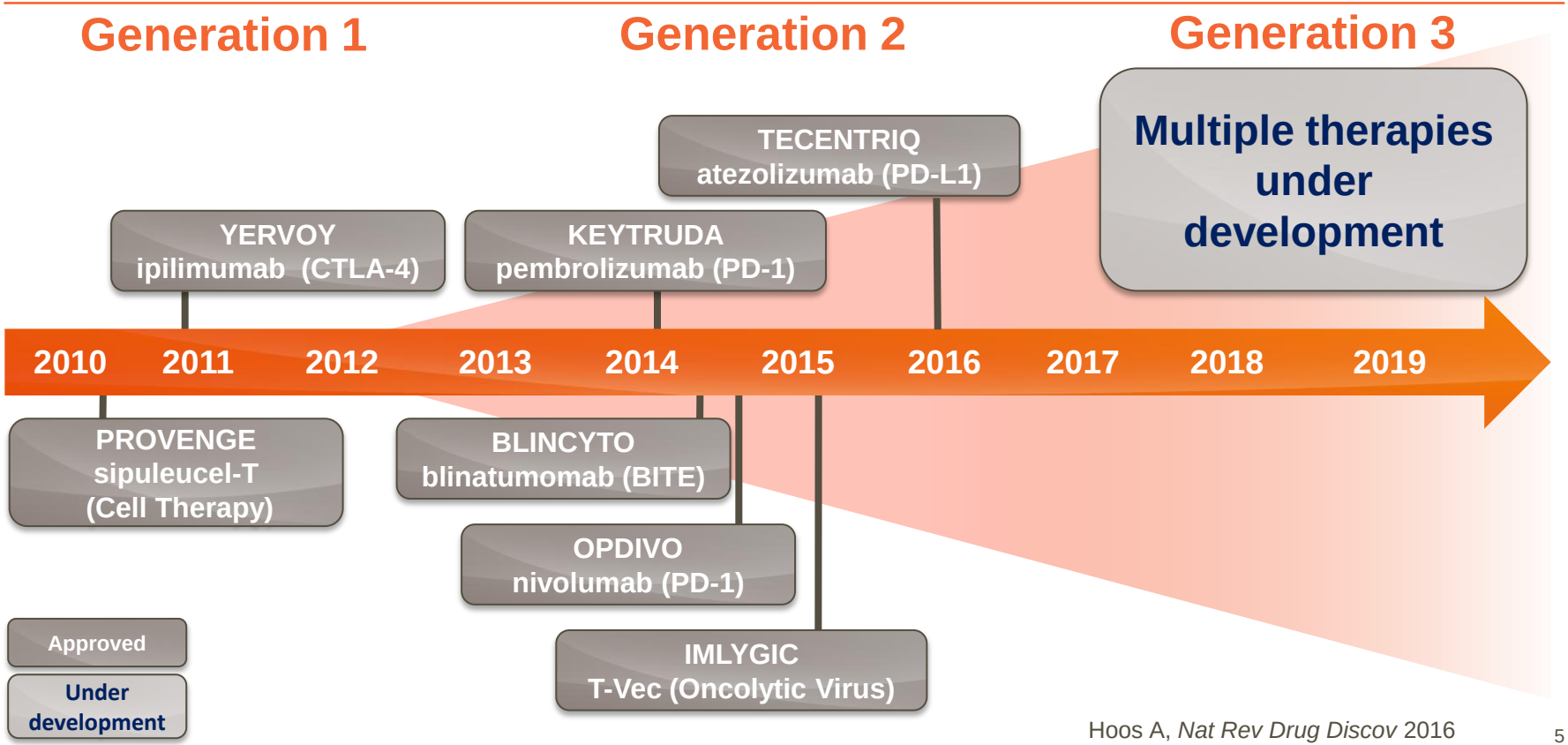
Oncology – Pipeline Snapshot

OX40 agonist (GSK3174998) †	*Solid tumours, Heme Malignancies*
ICOS agonist (GSK3359609) †	*Solid tumours*
BCMA ADC (GSK 2857916) †	*Multiple Myeloma*
TLR4 agonist (GSK1795091)	*Cancer*
Novel small molecule targets	
ImmTacs †	
mAb-dAbs and dual-specific Abs	
BET inhibitor (GSK525762)	*Solid tumours, Heme Malignancies*
LSD-1 inhibitor (GSK2879552)	*AML, SCLC*
EZH2 inhibitor (GSK2816126)	*Solid tumours, Heme Malignancies*
PRMT5 inhibitor (GSK3326595) †	*Solid tumours, Lymphoma*
PI3K beta inhibitor (GSK2636771)	*Prostate cancer*
Novel small molecule targets	
NY-ESO-1 TCR-T †	*Sarcoma, Multiple Myeloma, NSCLC, Ovarian cancer, Melanoma*
CAR-T and TCR-Ts	
Notch2/3 (tarextumab) †	*SCLC*

Immuno-Oncology
Epigenetics
Cell & gene therapy
Other targeted therapies

† Collaboration with a third party.

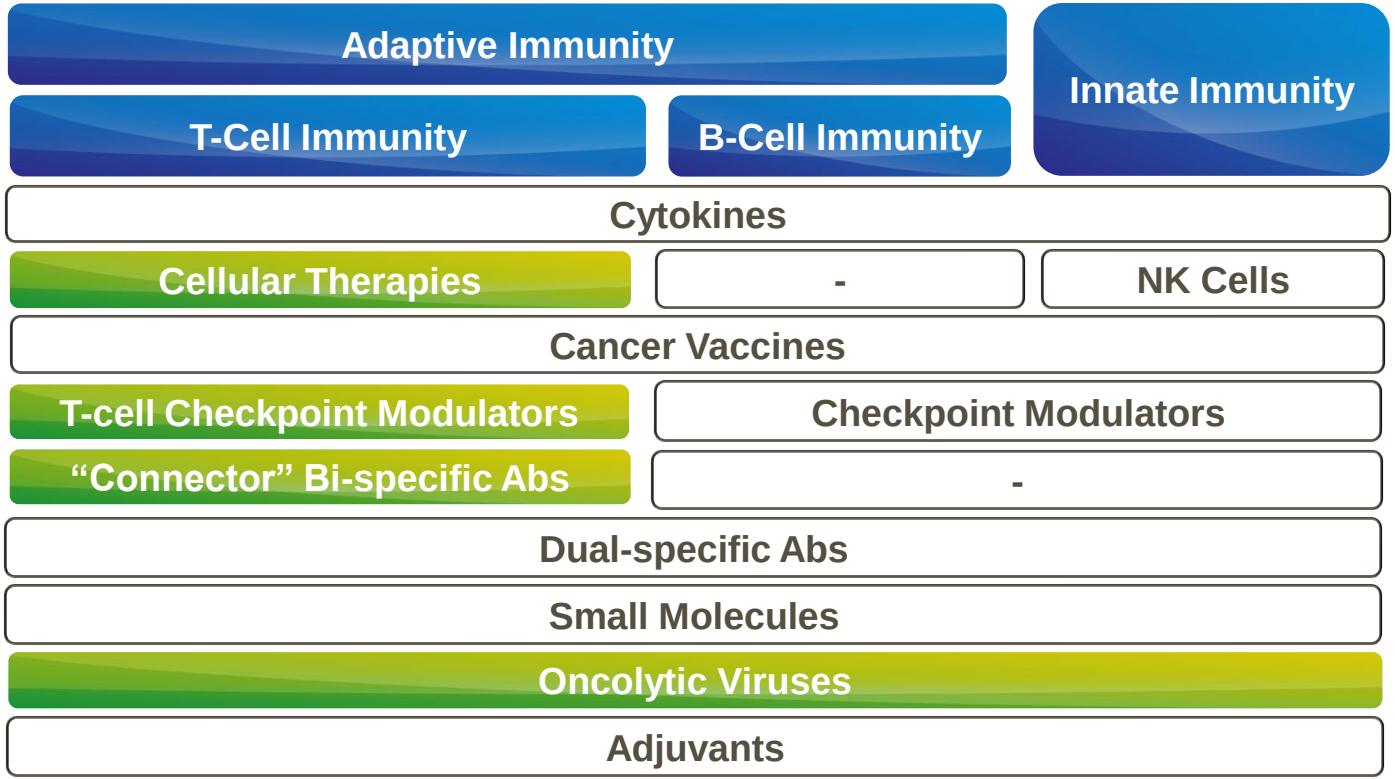
Immuno-Oncology: 3 Generations of Therapies



Hoos A, *Nat Rev Drug Discov* 2016

3rd Generation Opportunities

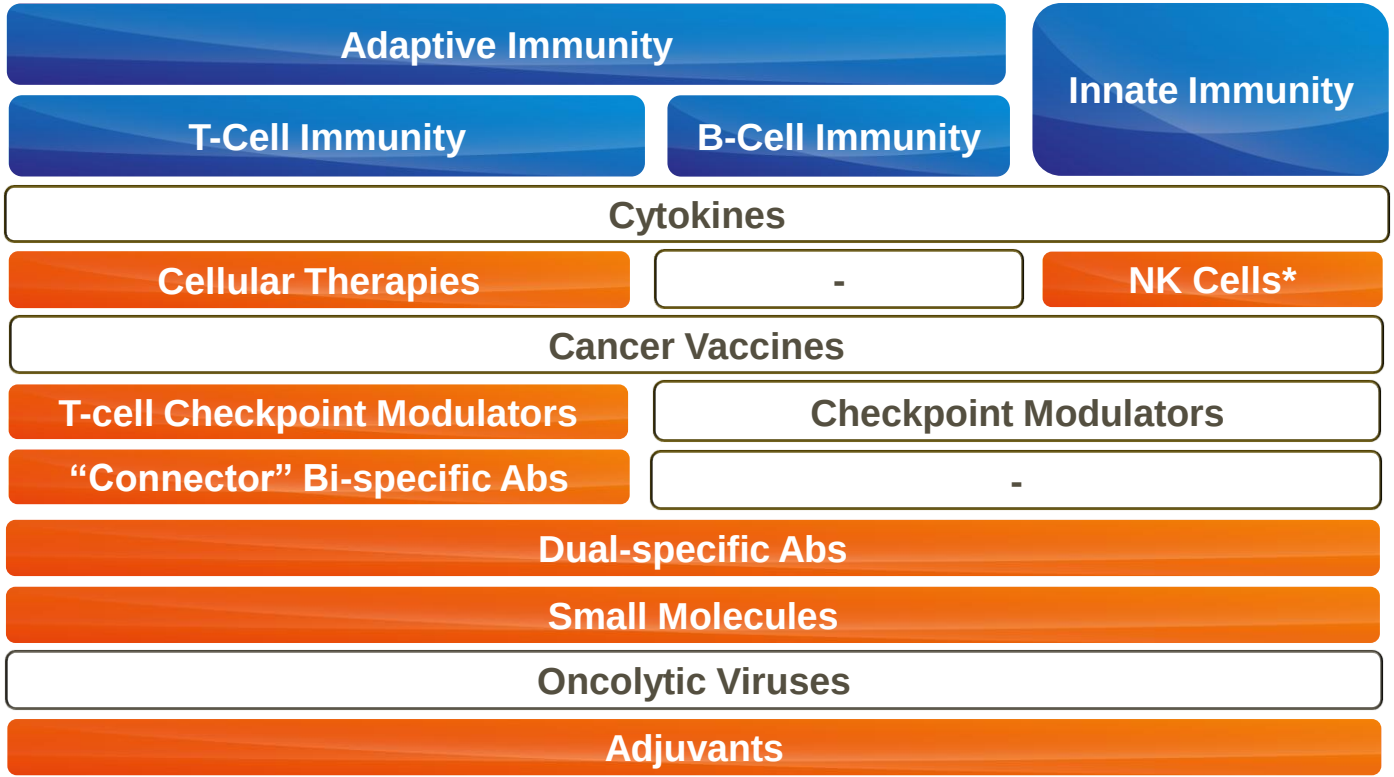
Spectrum of immuno-oncology modalities



Approved therapies

3rd Generation Opportunities

GSK's multi-modality pipeline



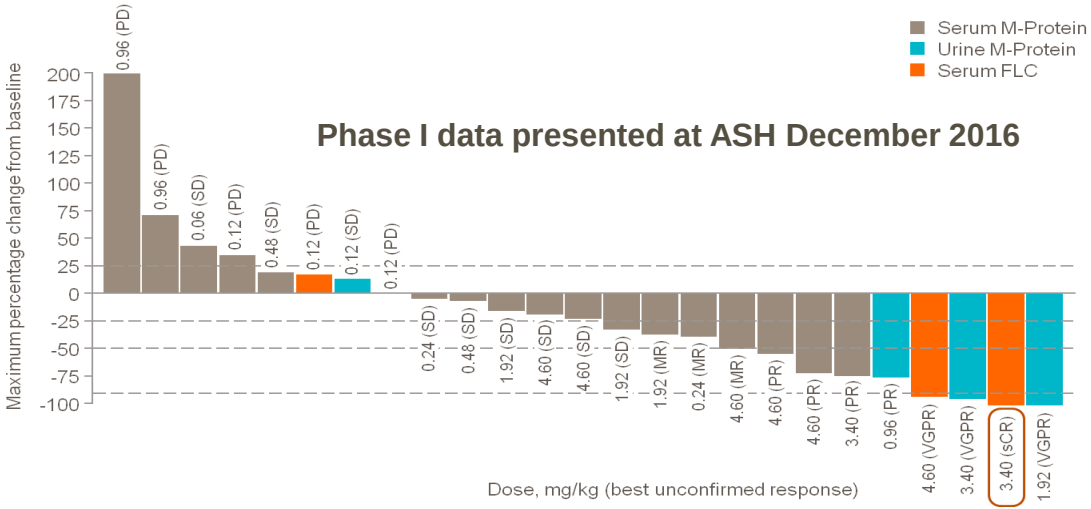
GSK Pipeline * in planning

GSK2857916: First-in-class anti-BCMA-ADC, proof of concept in multiple myeloma

- B Cell maturation antigen (BCMA)
- High-expression target in multiple myeloma and some NHL
- Antibody drug conjugate (ADC) with MMAF (auristatin derivative)
- Immunogenic cell death inducer
- Phase I efficacy in refractory population: ~67% RR at ≥ phase II dose
- Next steps:
  - Rapid development for monotherapy
  - Combinations with SOC and novel agents

All doses: ORR = 8/30 (27%; 95% CI: 12.3%, 45.9%)

At ≥Ph2 dose 3.4 mg/kg: ORR= 6/9 (66.7%; 95% CI: 0.29, 0.92%)

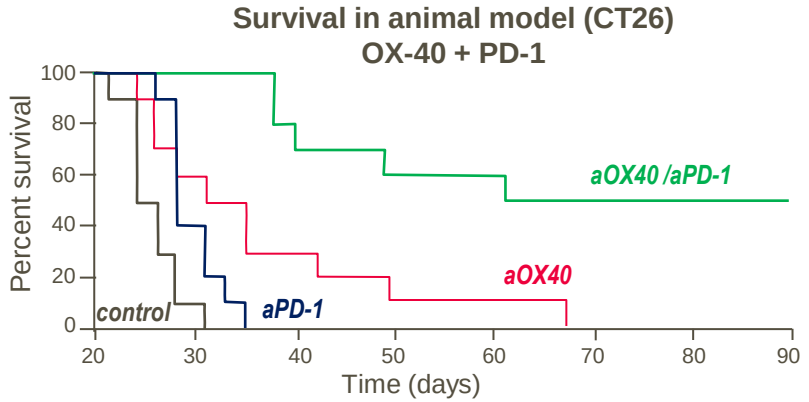


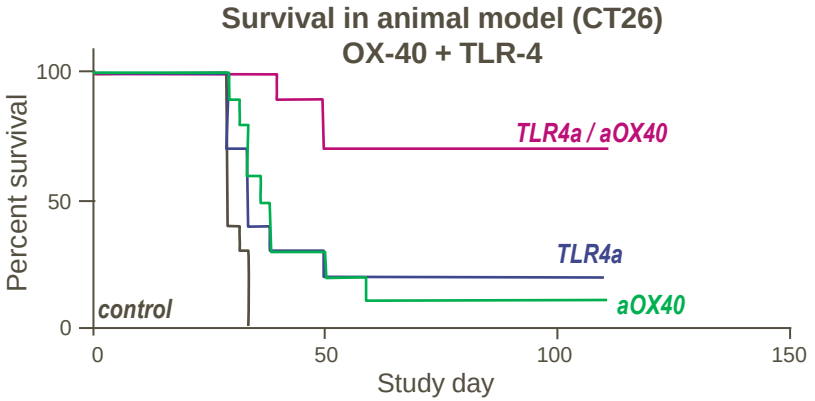
Safety observations:
Thrombocytopenia, transient
Corneal toxicity: dry eye, blurry vision, reversible

ASH: American Society of Hematology.

GSK3174998 OX40 agonist mAb

- GSK3174998 is one of several OX-40s in clinic
- Dual mechanism: enhancing effector T-cell and suppressing T-regs
- Collaboration with MD Anderson
- Phase I Study under way in eight cancers
- Combination with Merck PD1 started 3Q16
- Combination with GSK TLR4 expected to start in 2H2017



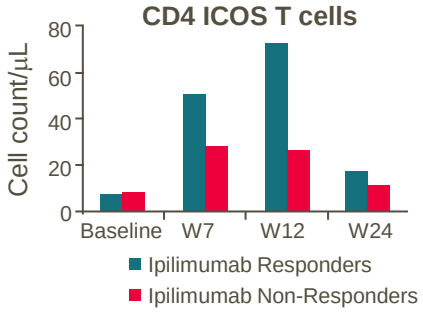


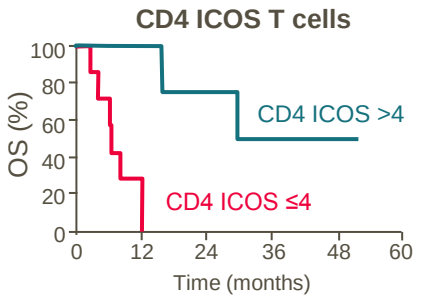
Source: GSK, data on file.

GSK3359609 First-in-class ICOS agonist mAb

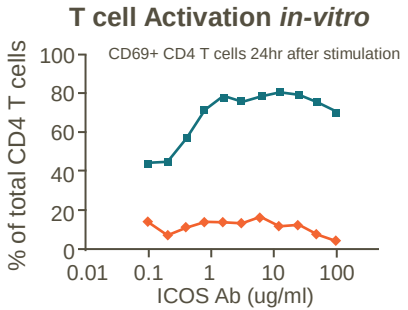
- Uniquely engineered IgG4 mAb with agonist function and no cell depletion
- Evolved from patient selection biomarker
- Enhances T-cells associated with clinical benefit
- Universal mechanism across multiple cancers: Phase I ongoing in 8 cancers
- Possible use after CTLA-4 and PD-1 in unresponsive or refractory patients
- Possible anchor for combinations: Expected start in combo with Merck PD-1 in 2Q17

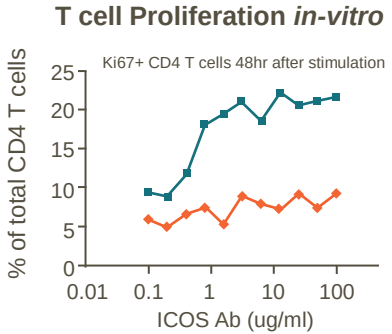
ICOS in ipilimumab-treated patients





GSK3359609



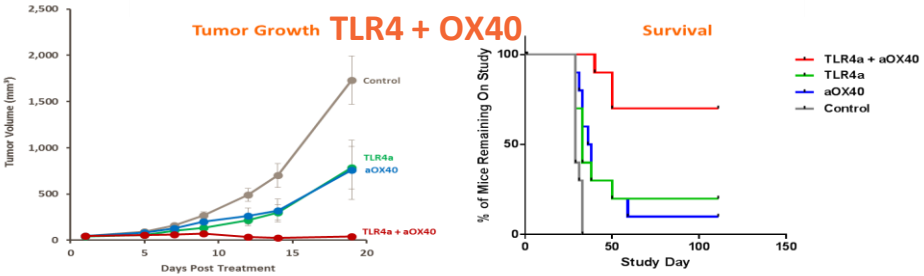


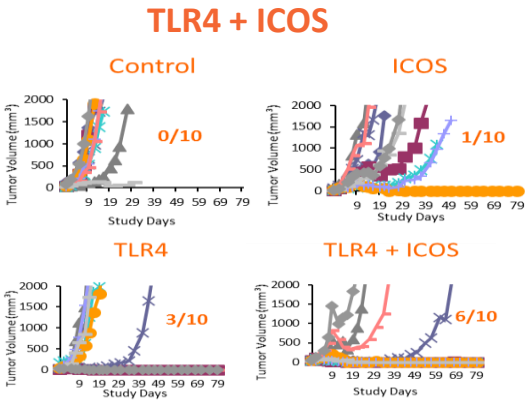
DiGiacomo, Clin Immunol Immunother 2013

GSK1795091: TLR4 agonist

- Glycolipid TLR-4 agonist compound
- Activates dendritic cells and innate immunity, positively modulates tumour microenvironment
- Strong combination potential with several IO agents
- Potential mechanistic synergies with OX40 and ICOS agonist mAbs
- Phase I in healthy volunteers under way to determine dose and PD effects
- Phase I combination with OX-40 in cancer patients expected to start 2H17

Pre-clinical combination synergy

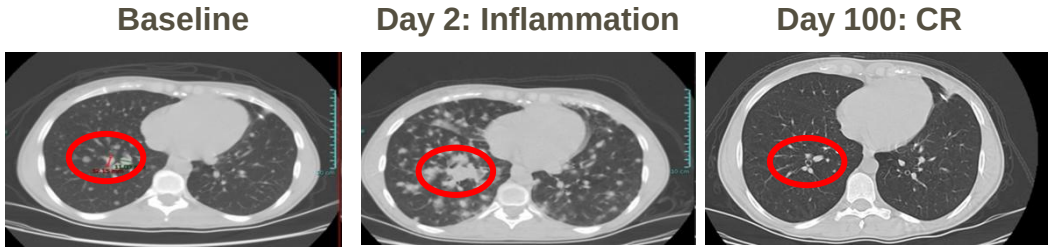




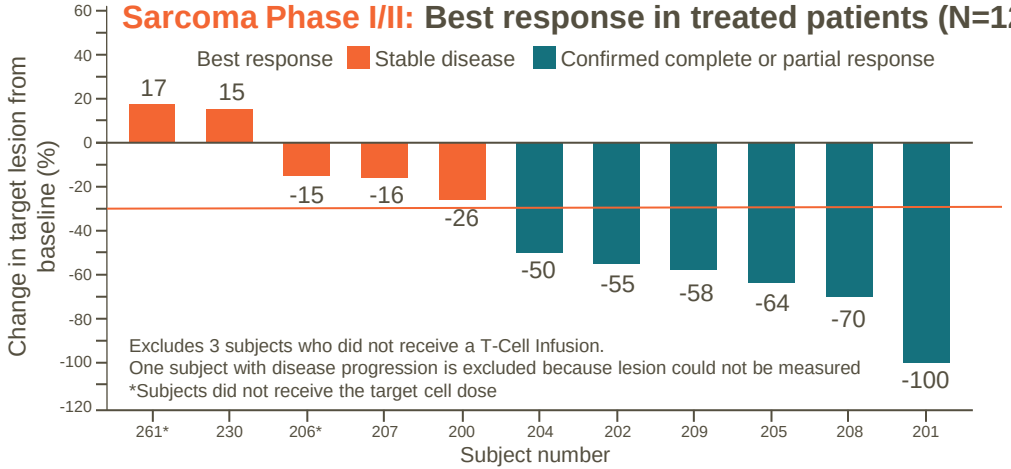
NY-ESO-1 TCR-T Cell Therapy

- TCR T-cell therapy
- 50% ORR in synovial sarcoma
- Ongoing studies in myeloma, ovarian cancer and other solid tumours
- Planned studies in combination with checkpoint modulators
- FDA Breakthrough designation
- EMA PRIME designation
- Collaboration with Adaptimmune

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



Sarcoma Phase I/II: Best response in treated patients (N=12)*



Note: GSK3377794 subject to exercise of option by GSK

Source: GSK, data on file.

Partnerships

GSK partnerships in Cell Therapy and Clinical Translational Research

Cell Therapy

Adaptimmune
TRANSFORMING T CELL THERAPY

MACS
Miltenyi Biotec

Perelman School of Medicine
University of Pennsylvania

iget
ISTITUTO SAN RAFFAELE TELETHON PER LA TERAPIA GENICA

MOLMED

And others…

Oncology Clinical & Translational Consortium

Memorial Sloan-Kettering Cancer Center

NKI-AVL

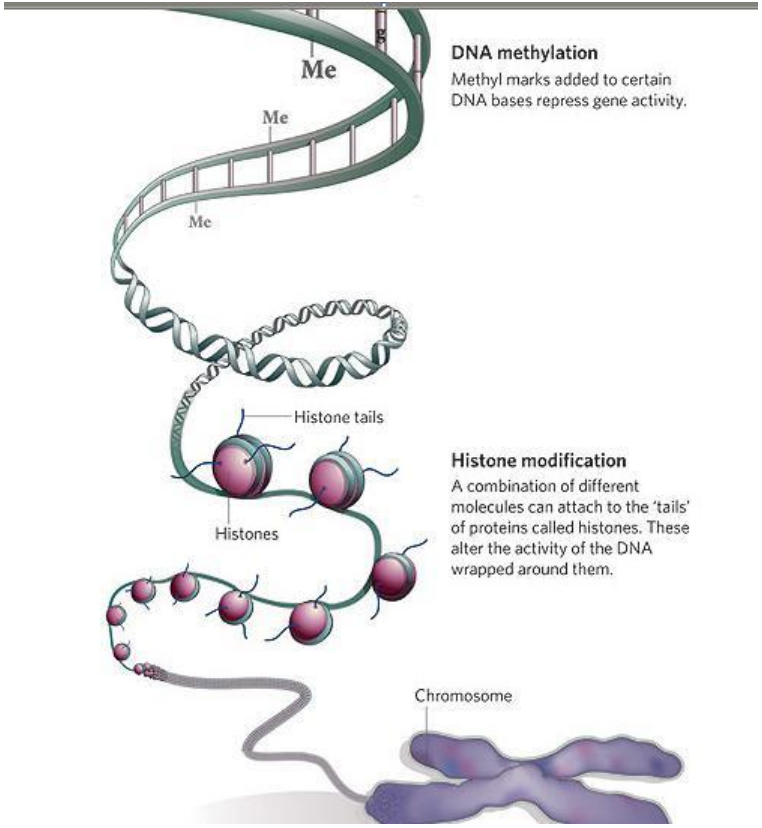
The Princess Margaret Cancer Centre
University Health Network

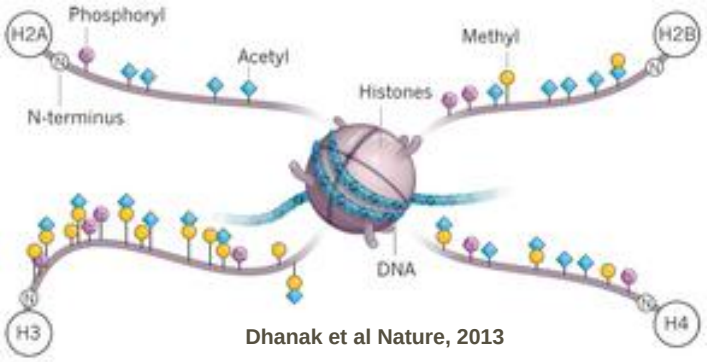
GUSTAVE ROUSSY
CANCER CAMPUS GRAND PARIS

VHIO
VALL D'HEBRON
Institute of Oncology

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Epigenetics clinical programs





Dhanak et al Nature, 2013

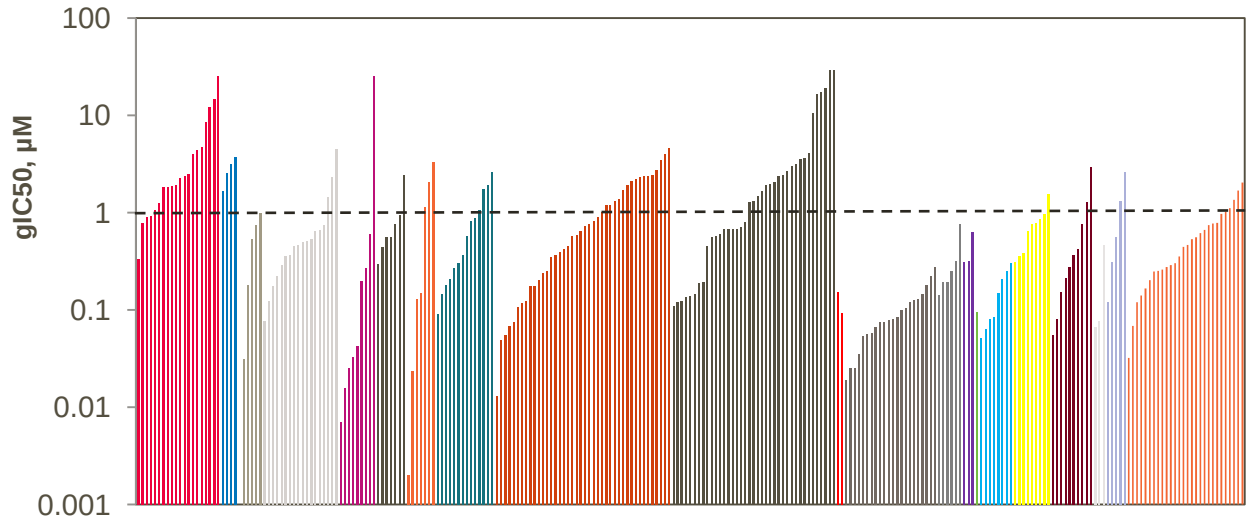
Erasing	Writing	Reading
Demethylases Deacetylases Phosphatases	Methyltransferases Acetyltransferases Kinases	Bromodomains Chromodomains Tudordomains
LSD1	EZH2 PRMT5	BET

GSK525762: BET inhibitor

Broad activity across multiple tumor types – preclinical cell line models

‘762 Blocks binding of BET family proteins (BRD2, 3 and 4) to acetylated histones causing targeted changes in gene expression including oncogene silencing

Preclinical data: Activity of GSK525762 in many cancer types (gIC50 < 1 μM)



Nature 2010;468:1119-1123

GSK525762: Potential First-in-class BET Inhibitor

Early clinical efficacy in NMC; Progress in many tumour types

Preliminary evidence of clinical activity in NUT midline carcinoma (NMC) (AACR 2016)

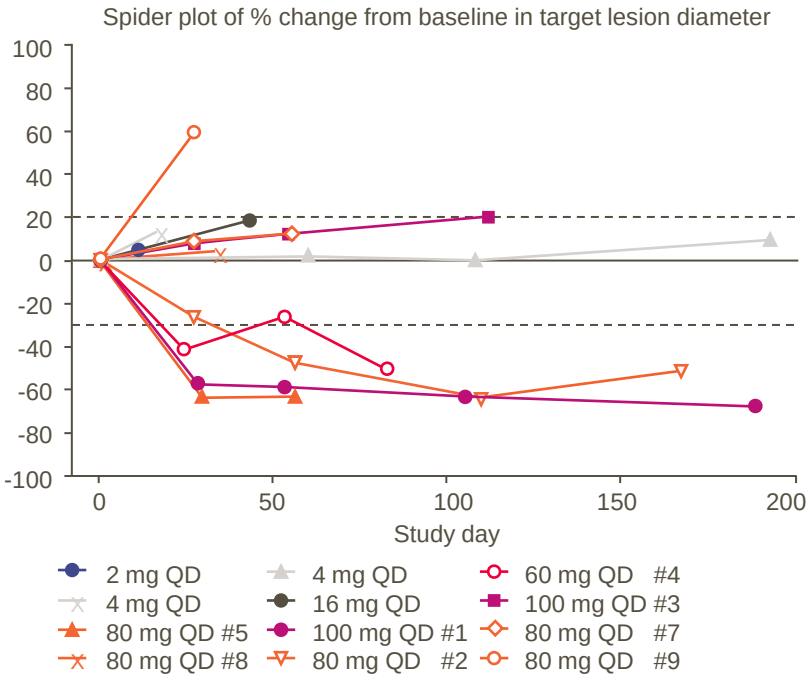
- Across all dose cohort (n=17):12% RR
- At 80/100 mg doses (n=9): 22% RR

Progress in Ph I since AACR 2016

- Solid Tumor: CRPC and ER positive BC expansion cohorts completed; TNBC, SCLC, NMC cohorts ongoing
- Heme: Dose finding in AML completed; dose finding in NHL and MM ongoing; expansion cohorts commencing April 2017
  - Anticipate presenting heme clinical data by YE 2017

Expect start of combination studies in 2017

- Pre-clinical data suggest combination synergy
- Combo in ER positive BC with fulvestrant (active)
- Combo in mCRPC with abiraterone or enzalutamide (start ~2Q)
- Other novel combos in 2017 and 2018



12 / 17 patients with NMC presented (5 non-evaluable).

Oncology at GSK

Mission: Maximise patient survival

Achieve a long-term leadership position in Oncology

Scientific Focus

- **Optimise T-cell Immunity**
- **Re-program cancer cells**
- **Cells as medicines**
- **Synergies and transformational effects through combinations**

Tactics

- **Diversified pipeline**
  - Across key modalities
- **Innovation**
  - 3rd 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**