Immuno-Oncology

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Senior Vice President, Oncology R&D

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Oncology R&D strategy

Focusing on 3 areas fundamental to oncology

Cancer Epigenetics
Immuno-Oncology
Cancer Stem Cells & Targeted Therapies

GSK Pipeline

- Long-Term Survival & Cures
- Reprogram Cancer Cells
- Stimulate Anti-Tumour Immunity
- First in Class Medicines & Combination Therapy
3 Generations of therapies

**Generation 1**

- **YERVOY** ipilimumab (CTLA-4)

**2010**

- **PROVENGE** sipuleucel-T (Cell Therapy)

**2011**

- **BLINCYTO** blinatumomab (BITE)

**2012**

- **OPDIVO** nivolumab (PD-1)

**2013**

- **KEYTRUDA** pembrolizumab (PD-1)

**2014**

- **IMLYGIC** T-Vec (Oncolytic Virus)

**2015**

- **KEYTRUDA** pembrolizumab (PD-1)

**2016**

- **CAR-Ts**

**2017**

- **Anti-PD-L1**

**2018**

- **CAR-Ts**

**2019**

- **Multiple therapies under development**

**2010**  **2011**  **2012**  **2013**  **2014**  **2015**  **2016**  **2017**  **2018**  **2019**

**Key**

- Approved
- Under development
Main trends

SOC replacements
Elimination of chemotherapy from SOC regimens

Immune profiling
Patient selection to predict response

New technologies
Expansion of the toolbox

2016

Substantial survival improvements
Across wide populations

Improved endpoints
Accelerated development

Complex combinations
Maximise efficacy

Improved endpoints
Accelerated development
3rd Generation opportunities

Spectrum of immuno-oncology modalities

- Adaptive Immunity
- Innate Immunity
- T-Cell Immunity
- B-Cell Immunity

Cytokines

Cellular Therapies - NK Cells

Cancer Vaccines

T-cell Checkpoint Modulators Checkpoint Modulators

“Connector” Bi-specific Abs -

Dual-specific Abs

Small Molecules

Oncolytic Viruses

Adjuvants

Approved therapies
3rd Generation opportunities

GSK’s multi-modality pipeline

Adaptive Immunity

T-Cell Immunity

B-Cell Immunity

Innate Immunity

Cytokines

Cellular Therapies

- NK Cells*

Cancer Vaccines

T-cell Checkpoint Modulators

Checkpoint Modulators

“Connector” Bi-specific Abs

Dual-specific Abs

Small Molecules

Oncolytic Viruses

Adjuvants

* in planning
### 3rd Generation leadership

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

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

* 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

**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
GSK3174998 OX40 agonist mAb

- GSK3174998 is one of four humanised OX-40s in clinic
- Dual mechanism: enhancing effector T-cell and suppressing T-reggs
- 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

GSK, data on file.
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

ICOS in ipilimumab-treated patients

<table>
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<tr>
<th>Time (months)</th>
<th>Baseline</th>
<th>W7</th>
<th>W12</th>
<th>W24</th>
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<td>CD4 ICOS T cells</td>
<td>100</td>
<td>90</td>
<td>80</td>
<td>70</td>
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T cell Activation in-vitro

- CD69+ CD4 T cells 24hr after stimulation

<table>
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<tr>
<th>ICOS Ab (ug/ml)</th>
<th>CD69+ CD4 T cells</th>
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<tbody>
<tr>
<td>0.01</td>
<td>50</td>
</tr>
<tr>
<td>0.1</td>
<td>45</td>
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<tr>
<td>10</td>
<td>35</td>
</tr>
<tr>
<td>100</td>
<td>30</td>
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</tbody>
</table>

T cell Proliferation in-vitro

- Ki67+ CD4 T cells 48hr after stimulation

<table>
<thead>
<tr>
<th>ICOS Ab (ug/ml)</th>
<th>Ki67+ CD4 T cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>5</td>
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<tr>
<td>0.1</td>
<td>10</td>
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<tr>
<td>1</td>
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<tr>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>100</td>
<td>25</td>
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</table>

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

DiGiacomo, Clin Immunol Immunother 2013
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)
# Immuno-Oncology at GSK

**Mission:** Maximise patient survival  
**Achieve a long-term leadership position in Oncology**

<table>
<thead>
<tr>
<th>Scientific Focus</th>
<th>Tactics</th>
<th>Goals</th>
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</table>
| • Optimise T-cell Immunity  
Rationale: has delivered transformational medicines                                | • 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                  | • Transformational effects for patients  
• Maximise survival  
• Pipeline sustainability  
• Long-term leadership position in Oncology                                         |
| • Synergies and transformational effects through combinations                      | • Partnerships  
• Best science  
• Access to combinations                                                           |                                                                                         |