GSK ‘916: anti-BCMA ADC

An exciting potential advance in the treatment of Multiple Myeloma

12 December 2017
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A number of adjusted measures are used to report the performance of our business. These measures are defined in our Q3 2017 earnings release and Annual Report on Form 20-F for 2016.

All expectations and targets regarding future performance should be read together with “Assumptions related to 2017 guidance and 2016-2020 outlook” on page 34 of our Q3 earnings release.

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Agenda

Multiple Myeloma market
Luke Miels
President, Global Pharmaceuticals

‘916, a priority asset in GSK oncology pipeline
Axel Hoos, MD, PhD
SVP and Head of Oncology Therapy Area

Results of DREAMM-1 study
Paul Richardson, MD
Medical Oncology, Dana Farber Cancer Institute

Presentation
20-25 mins

Q&A
20-25 mins
Developing the pipeline in Pharma

Development capital focus on 2 core and 2 potential therapy areas

**Capital**

80%  
20%

**Therapy Areas**

- Respiratory
- HIV/Infectious diseases
- Immuno-inflammation
- Oncology
- Future pipeline optionality

**Prioritised assets**

- *Trelegy* (closed triple)  
  PI3Kδ danirixin
- *Juluca* (DTG+rilpivirine)  
  DTG+lamivudine cabotegravir + rilpivirine
- tapinarof  
  RIP-1  
  anti-GM-CSF
- BCMA  
  NY- ES0-1  
  BET  
  OX-40  
  ICOS
- daprodustat  
  anti-SAP
Multiple Myeloma (MM): An incurable hematologic malignancy with high unmet medical need, despite new treatments

**Disease background**

- Second most common blood cancer
- Myeloma affects major organs of the body which leads to bone disease (~75%), renal compromise, anaemia and infection
- Not curable
- Estimated incidence:
  - Global: 124,000
    - US: 30,000
    - EU5 27,000
    - Japan 8,000

**5-year survival data**

(>most recent survival data available: does not reflect most recent innovations)

Kumar, S. et al., Leukemia (2014)
Aging population – increasing incidence
- Longer duration of therapy, multiple lines
- Innovation
  - Efficacy remains key driver of acceptance of new agents
  - Darzalex‡ (daratumumb anti-CD38 mAb) among a new class, gaining acceptance due to efficacy profile vs previous standard of care (SoC)
  - High interest in new interventions, targets and modalities, including ‘916, CAR-Ts
- Shift towards combination therapies

Market value ~$12bn in 2016, +40% vs 2015

Growth expected to continue: +16% CAGR 2016-22 to $29bn¹

Fragmented treatment paradigm*

Opportunity for new entrants

1\textsuperscript{st} Line patients needing therapy

Transplant-Ineligible (TI) 55-60%

Transplant-Eligible (TE) 40-45%

2\textsuperscript{nd} Line

3\textsuperscript{rd} Line

4\textsuperscript{th} Line

5\textsuperscript{th} Line+

1\textsuperscript{st} Line therapy (followed by maintenance)

- Velcade\textsuperscript{†} / Revlimid\textsuperscript{‡} (Thalomid\textsuperscript{†}) / Dex based regimens (SoC);
- VelRevDex\textsuperscript{‡} preferred (US);
- VelMelPrednisone\textsuperscript{‡} (TI; Ex US)

Switch/Re-treat 1\textsuperscript{st} Line regimen

2\textsuperscript{nd} gen Proteasome Inhibitor (Kyprolis\textsuperscript{‡}, Ninlaro\textsuperscript{‡}) ± RevDex\textsuperscript{‡}

DarzalexRevDex\textsuperscript{‡}; DarazalexVelDex\textsuperscript{‡}; EmplicitiRevDex\textsuperscript{‡}

- PomDex\textsuperscript{‡}; DarzalexPomDex\textsuperscript{‡};
- EmplicitiRevDex\textsuperscript{‡}; Kyprolis\textsuperscript{‡}± Dex

Darzalex\textsuperscript{‡}; PomDex\textsuperscript{‡};

Treatments that have not been used before

- Best Supportive Care,
- Clinical trial

\*Source: GSK Market Research based on various publications and treatment guidelines. Regimen preference vary by regions and patient performance status; Maintenance therapy is mostly in the US
Oncology R&D
Maximising survival through transformational medicines and combinations

Immuno-Oncology

Cell & Gene Therapy
Reprogram cancer cells
Stimulate anti-tumour immunity
Cells as medicines

Cancer Epigenetics

GSK pipeline
Long-term survival & cures
First-in-class medicines
Combination therapy

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## Innovative & emerging oncology pipeline

BCMA is the lead asset

<table>
<thead>
<tr>
<th>Mechanism Pre-clinical</th>
<th>Phase I</th>
<th>Phase II</th>
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</thead>
<tbody>
<tr>
<td><strong>Immuno-Oncology</strong></td>
<td></td>
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<tr>
<td>BCMA ADC (GSK 2857916)</td>
<td>Heme malignancies</td>
<td></td>
</tr>
<tr>
<td>ICOS agonist (GSK3359609)</td>
<td>Solid tumours</td>
<td></td>
</tr>
<tr>
<td>OX40 agonist (GSK3174998)</td>
<td>Solid and heme malignancies</td>
<td></td>
</tr>
<tr>
<td>TLR4 agonist (GSK1795091)</td>
<td>Cancer</td>
<td></td>
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<tr>
<td>Novel small molecule targets</td>
<td></td>
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<tr>
<td>ImmTacs</td>
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<td></td>
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<tr>
<td>Bi-specific Abs</td>
<td></td>
<td></td>
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<tr>
<td><strong>Cancer Epigenetics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BET inhibitor (GSK525762)</td>
<td>Solid tumours, heme malignancies</td>
<td></td>
</tr>
<tr>
<td>PRMT5 inhibitor (GSK3326595)</td>
<td>Solid tumours, lymphoma</td>
<td></td>
</tr>
<tr>
<td>PI3K beta inhibitor (GSK2636771)</td>
<td>Prostate cancer</td>
<td></td>
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<tr>
<td>Novel small molecule targets</td>
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<td></td>
</tr>
<tr>
<td><strong>Cell &amp; Gene Therapy</strong></td>
<td>Sarcoma, solid and heme malignancies</td>
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<tr>
<td>NY-ESO-1 TCR-T</td>
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<tr>
<td>CAR-T and TCR-Ts</td>
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† Collaboration with a third party.
First-in-class anti-BCMA agent with multiple modes of action

The agent
- GSK’916 is a humanised IgG1 antibody targeting BCMA (B-cell maturation antigen)
  - Linked to the anti-mitotic agent MMAF
  - Afucosylated to enhance ADCC

The target
- BCMA plays a key role in plasma cell survival
  - It is found on the surfaces of plasma cells and is overexpressed on malignant plasma cells
  - Not expressed in healthy tissues

Key attributes
- New modality in multiple myeloma: first ADC
  - Easy and convenient to administer: 1h infusion q3w
  - No pre-medications for infusion reactions
    - Pre-medications with steroid eye drops
  - New MoA enabling diverse combinations

Four mechanisms of action:
1. ADC mechanism
2. ADCC mechanism
3. BCMA receptor signaling inhibition
4. Immunogenic cell death

ADC, antibody-drug conjugate; ADCC, antibody-dependent cell-mediated cytotoxicity; BCMA, B-cell maturation antigen; MMAF, monomethyl auristatin-F
DREAMM-1: study design

**DRiving Excellence in Approaches to Multiple Myeloma**

- Patients enrolled *regardless of BCMA expression levels*
- **No dose limiting toxicities** observed in dose finding phase - 38 patients with relapsed/refractory multiple myeloma
- Expansion phase:
  - Cohort 1: relapsed/refractory MM (enrolment complete); data presented at 59th ASH Annual Meeting (Dec 2017)
    - 57% had **5+ prior lines of treatment**
  - Cohort 2: BCMA-positive relapsed DLBCL or follicular lymphoma (enrolment ongoing)

<table>
<thead>
<tr>
<th>Dose finding phase</th>
<th>Expansion phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>completed</strong></td>
<td><strong>ongoing</strong></td>
</tr>
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</table>

### Dose finding phase

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>N</th>
</tr>
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<tbody>
<tr>
<td>0.03</td>
<td>1</td>
</tr>
<tr>
<td>0.06</td>
<td>1</td>
</tr>
<tr>
<td>0.12</td>
<td>4</td>
</tr>
<tr>
<td>0.24</td>
<td>4</td>
</tr>
<tr>
<td>0.48</td>
<td>4</td>
</tr>
<tr>
<td>0.96</td>
<td>3</td>
</tr>
<tr>
<td>1.92</td>
<td>4</td>
</tr>
<tr>
<td>3.4</td>
<td>3</td>
</tr>
<tr>
<td>4.6</td>
<td>6</td>
</tr>
</tbody>
</table>

*N=38

### Expansion phase

**Cohort 1:** 3.4 mg/kg (enrolment completed)  
*N=35

**Cohort 2:** 3.4 mg/kg (enrolment ongoing)  
*N≈10

ASH 2016

ASH 2017

DLBCL: diffuse large B-cell lymphoma
### DREAMM-1 Part 2: Demographics and baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Part 2 (N=35)</th>
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</thead>
<tbody>
<tr>
<td>Age (years), median (min, max)</td>
<td>60 (46–75)</td>
</tr>
<tr>
<td>Females/males, %</td>
<td>51/49</td>
</tr>
<tr>
<td>≥5 prior lines, n (%)</td>
<td>20 (57)</td>
</tr>
<tr>
<td>ASCT</td>
<td>31 (89)</td>
</tr>
<tr>
<td><strong>IMiDs, n (%)</strong></td>
<td>35 (100)</td>
</tr>
<tr>
<td>- Lenalidomide</td>
<td>33 (94)</td>
</tr>
<tr>
<td>- Pomalidomide</td>
<td>21 (60)</td>
</tr>
<tr>
<td>- Thalidomide</td>
<td>12 (34)</td>
</tr>
<tr>
<td><strong>Refractory to IMiD</strong></td>
<td>32 (91)</td>
</tr>
<tr>
<td><strong>Pl, n (%)</strong></td>
<td>35 (100)</td>
</tr>
<tr>
<td>- Bortezomib</td>
<td>34 (97)</td>
</tr>
<tr>
<td>- Carfilzomib</td>
<td>28 (80)</td>
</tr>
<tr>
<td><strong>Refractory to Pl, n (%)</strong></td>
<td>34 (97)</td>
</tr>
<tr>
<td><strong>Daratumumab, n (%)</strong></td>
<td>14 (40)</td>
</tr>
<tr>
<td><strong>Refractory to daratumumab, n (%)</strong></td>
<td>13 (37)</td>
</tr>
<tr>
<td><strong>Refractory to IMiD/Pl, n (%)</strong></td>
<td>31 (89)</td>
</tr>
<tr>
<td><strong>Refractory to IMiD/Pl and prior daratumumab, n (%)</strong></td>
<td>12 (34)</td>
</tr>
<tr>
<td><strong>Cytogenetics risk, n (%)</strong></td>
<td></td>
</tr>
<tr>
<td>- High risk</td>
<td>10 (29)</td>
</tr>
<tr>
<td>- Other (non-high risk, not done, or missing)</td>
<td>25 (71)</td>
</tr>
</tbody>
</table>

ASCT, autologous stem cell transplant; IMiD, immunomodulator; Pl, proteasome inhibitor

*Patients with any of the following genetic abnormalities were considered high risk: t(4:14), del17, t(14:16), t(14:20), nonhiperdiplody, or gain 1q
Transformational efficacy in multiple myeloma: ORR

Overall ORR = 60% 95%CI (42.1%,76.1%); n=35

Patients refractory to IMID and PI (n=31) ORR=58% [95%CI (39.1%,75.5%)]

Patients previously treated with daratumumab (n=14) ORR=43% [95%CI (17.7%,71.1%)]
DREAMM-1 Part 2: Response characteristics

- Early response seen after 1-2 doses
- Mostly durable
- Dose reductions did not lead to loss of response

CR, complete response; PD, progressive disease; PR, partial response; sCR, stringent complete response; VGPR, very good partial response
DREAMM-1 Part 2: Efficacy – progression-free survival and duration of response

**Progression free survival**
- Number of subjects: 35
  - Progressed or died: 15 (43%)
  - Censored, f/u ended: 3 (9%)
  - Censored, f/u ongoing: 17 (49%)

  **Q1 (95% CI)**: 2.3 (0.7, 6.8)
  **Median (95% CI)**: 7.9 (3.1, -)
  **Q3 (95% CI)**: N/A

**Duration of response**
- Number of subjects: 21
  - Progressed or died: 4 (19%)
  - Censored, f/u ended: 0
  - Censored, f/u ongoing: 17 (81%)

  **Q1 (95% CI)**: 6.7 (1.6, -)
  **Median (95% CI)**: N/A (6.7, -)
  **Q3 (95% CI)**: N/A
Most frequent adverse events
• Corneal events 63%
• Thrombocytopenia 49%

Corneal events - mostly low grade (9% G3)
• Manageable with steroid eye drops
• Dose reductions

Hematologic AEs (including thrombocytopenia)
• Frequent in MM population due to disease

Infusion Related Reactions (IRR) 23%
• Occur at first dose without premedication
• Manageable
• Do not recur with subsequent doses
**GSK’916 single agent has transformational efficacy**

<table>
<thead>
<tr>
<th>Drug, Sponsor</th>
<th>Line of Therapy; Trial</th>
<th>ORR</th>
<th>mPFS</th>
<th>mOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>¹Kryprolis (IV), monotherapy Amgen</td>
<td>3L+, Single arm, N=266</td>
<td>23.7%</td>
<td>3.7m</td>
<td>15.6m</td>
</tr>
<tr>
<td>²Darzalex (IV), monotherapy Janssen</td>
<td>4L+, Single arm, N=106</td>
<td>29.2%</td>
<td>3.7m</td>
<td>17.5m</td>
</tr>
<tr>
<td>GSK’916 (IV), monotherapy</td>
<td>5 median lines (40% Darzalex treated), Single arm, N=35</td>
<td>60% (43% in Darzalex exposed)</td>
<td>7.9m (6.8m in Darzalex exposed)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Breakthrough therapy designation from FDA

EMA granted PRIME designation

Orphan drug designation from the EMA and FDA for multiple myeloma

Monotherapy in Multiple Myeloma
- Pivotal phase 2 start: 4th line
- Phase 1/2 start: 2nd line

Combination therapy with SOC in Multiple Myeloma
- Phase 1/2 start

Novel combination therapy in Multiple Myeloma

Lymphoma
- Phase 1/2 lymphoma cohort data readout & Phase 2 start

2018
- Pivotal phase 2 start: 4th line
- Phase 1/2 start: 2nd line

2019
- Pivotal data readout 4th line
- Data readout and pivotal trial start 2nd line

2020 +
- Filing & launch
- Data readout and pivotal trial start

Ongoing discussions with regulators
Novartis has a right of first negotiation (ROFN) that is triggered upon our decision to seek a partner or divest certain oncology assets or if we propose to seek a marketing authorization for such oncology assets, on an asset by asset basis.

NVS does not have an “opt-in” or a “call” option related to GSK’s oncology pipeline.

GSK’s obligation is to negotiate in good faith. GSK would only enter into a transaction if it believes that is in the best interests of its shareholders.

The ROFN does not oblige GSK to sell to, or partner with, NVS. The ROFN is not an obligation to consummate a transaction with NVS. Under the ROFN, we are able to continue to develop and commercialise assets on our own.

The ROFN extends for 12.5 years from closing of the original GSK/Novartis transactions; i.e. September 2027.

Not intended to provide a complete summary of all the terms of the ROFN. The contractual terms of the ROFN are available at https://www.sec.gov/Archives/edgar/data/1131399/000119312516510261/d32974dex410.htm