ESMO Investor call: accelerating our oncology pipeline

30 September 2019
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A number of adjusted measures are used to report the performance of our business, which are non-IFRS measures. These measures are defined and reconciliations to the nearest IFRS measure are available in our second quarter 2019 earnings release and Annual Report on Form 20-F for FY 2018.

All expectations and targets regarding future performance and the dividend should be read together with “Assumptions related to 2019 guidance and 2016-2020 outlook” on page 61 of our second quarter 2019 earnings release.
Agenda

Accelerating our oncology pipeline
Dr Hal Barron
Chief Scientific Officer, President R&D

Results of PRIMA
Dr Antonio González-Martín
Head of Medical Oncology, Clinica Universidad de Navarra

Putting PRIMA in context
Dr Hal Barron
Chief Scientific Officer, President R&D

Oncology strategy & data presentations at ESMO
Dr Axel Hoos
SVP, Oncology R&D

Building our in market oncology capabilities
Luke Miels
President, Global Pharmaceuticals

Q&A:
Christine Roth, SVP Global Oncology Therapy Area Head
Jenn Christensen, Medicine Development Lead niraparib
Dr Marc Ballas, Medicine Development Lead GSK’609
Science

Technology

Culture

Strengthening our R&D pipeline through a focus on science related to the immune system, the use of human genetics, and advanced technologies
**GSK Oncology: building on a strong foundation and investing for future performance**

<table>
<thead>
<tr>
<th>Smart business development</th>
<th>Strong internal R&amp;D capabilities</th>
<th>Strengthening in market operations</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Tesaro acquisition</td>
<td>- High calibre scientists within clinical teams</td>
<td>- Tesaro accelerated build of infrastructure</td>
</tr>
<tr>
<td>- Zejula expected to be supported by PRIMA</td>
<td>- Diverse portfolio of potentially transformational medicines</td>
<td>- Focus on recruiting the best sales force and medical talent</td>
</tr>
<tr>
<td>- Dostarlimab expected to file by end 2019</td>
<td>- Prioritisation and investment to accelerate promising assets including belantamab mafodotin, GSK’609</td>
<td>- Changed HCP engagement and sales rep incentivisation policies to be more competitive</td>
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<tr>
<td>- Early stage IO pipeline</td>
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<tr>
<td>- Merck KGaA global alliance on bintrafusp alfa (M7824)</td>
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</tr>
</tbody>
</table>

17 assets in oncology pipeline

16 abstracts across 9 tumour types at ESMO

Further important data expected at ASH’19 and ASCO’20

3 oncology filings expected by end 2019
GSK Oncology: building on a strong foundation and investing for future performance

**Smart business development**
- Tesaro acquisition
  - Zejula expected to be supported by PRIMA
  - Dostarlimab expected to file by end 2019
  - Early stage IO pipeline
- Merck KGaA global alliance on bintrufusp alfa (M7824)

**Strong internal R&D capabilities**
- High calibre scientists within clinical teams
- Diverse portfolio of potentially transformational medicines
- Prioritisation and investment to accelerate promising assets including belantamab mafodotin, GSK’609

**Strengthening in market operations**
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- Focus on recruiting the best sales force and medical talent
- Changed HCP engagement and sales rep incentivisation policies to be more competitive

17 assets in oncology pipeline
16 abstracts across 9 tumour types at ESMO
Further important data expected at ASH’19 and ASCO’20
3 oncology filings expected by end 2019
Results of PRIMA

Dr Antonio González Martín, Head of Medical Oncology, Clinica Universidad de Navarra
Niraparib is effective in recurrent ovarian cancer (\textit{BRCAmut} and \textit{BRCAwt})

- Advanced ovarian cancer is a leading cause of cancer deaths in women with up to 85% recurrence after completion of standard first-line platinum-based chemotherapy\(^1\)

- Despite current options for maintenance treatment, there is still a high unmet need for many patients
  - \textbf{Olaparib}: limited to patients with \textit{BRCA} mutations; \(\approx\)20\% of OC patients\(^2\)
  - \textbf{Bevacizumab}: limited use due to safety concerns and limited data in the growing number of patients receiving NACT
  - \textbf{Active surveillance}: many patients undergo watchful waiting following chemotherapy

- Niraparib was the first oral PARP inhibitor approved as maintenance for all patients with recurrent OC (\textit{BRCAmut} and \textit{BRCAwt})
  - NOVA study demonstrated efficacy of niraparib maintenance after platinum CT in all biomarker populations:
    \begin{itemize}
    \item \textit{gBRCA} mut: hazard ratio 0.27 (95\% CI 0.17–0.41, \(P<0.0001\)); homologous recombination deficient: hazard ratio 0.38 (95\% CI 0.24–0.59, \(P<0.0001\)) and non-\textit{gBRCA} mut: hazard ratio 0.45 (95\% CI 0.34–0.61, \(P<0.0001\))\(^3\)
    \end{itemize}
  - \textbf{QUADRA} study showed niraparib treatment benefit in patients with at least 3 prior therapies: \textit{BRCAmut} 39\% ORR, homologous recombination deficient 26\% ORR, duration of response 9.4 months\(^4\)

\footnotesize{CI, confidence interval; CT, chemotherapy; NACT, neoadjuvant chemotherapy; mut, mutant; OC, ovarian cancer; ORR, objective response rate; PARP, poly (ADP-ribose) polymerase; wt, wild-type.
PRIMA was designed to address the unmet need in 1L advanced ovarian cancer

**Hypothesis:** PRIMA/ENGOT-OV26/GOG-3012 was designed to test the efficacy and safety of niraparib therapy after response to platinum-based chemotherapy in patients with newly diagnosed advanced ovarian cancer, including those at high risk of relapse (ClinicalTrials.gov: NCT02655016)

<table>
<thead>
<tr>
<th>Key inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• High grade serous or endometroid pathology</td>
</tr>
<tr>
<td>• Stage III: PDS with visible residual disease post surgery, NACT, or inoperable</td>
</tr>
<tr>
<td>• Stage IV: PDS regardless of residual disease, NACT, or inoperable</td>
</tr>
<tr>
<td>• CR or PR following platinum first-line treatment</td>
</tr>
<tr>
<td>• Tissue for homologous recombination testing was required at screening (Myriad myChoice®)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Key exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patients with Stage III disease who have had complete cytoreduction (i.e., no visible residual disease) after PDS</td>
</tr>
</tbody>
</table>

CR, complete response, HRD, homologous recombination deficiency; NACT, neoadjuvant chemotherapy; OC, ovarian cancer; PDS, primary debulking surgery, PR partial response.
**PRIMA trial design**

**2:1 Randomization**

- **Niraparib**
- **Placebo**

**Endpoint assessment**

- **Primary Endpoint**: Progression-free survival by BICR
- **Key Secondary Endpoint**: Overall Survival
- **Secondary Endpoints**: PFS2, TFST, PRO, Safety

**Stratification Factors**

- Neoadjuvant chemotherapy administered: Yes or no
- Best response to first platinum therapy: CR or PR
- Tissue homologous recombination test status: deficient or proficient/not-determined

**Hierarchical PFS Testing**

- Body weight ≥77 kg and platelets ≥150,000/μL started with 300 mg QD
- Body weight <77 kg and/or platelets <150,000/μL started with

1L, first-line; BICR, blinded independent central review; CR, complete response; OC, ovarian cancer; OS, overall survival; PFS2, progression-free survival 2; PR partial response; PRO, patient-reported outcomes; TFST, time to first subsequent therapy.
**PRIMA tissue test for homologous recombination**

<table>
<thead>
<tr>
<th>Testing for Homologous Recombination Deficiency (HRd) and Proficiency (HRp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Next generation sequencing of DNA from tumor tissue (Myriad Genetics myChoice® Test)</td>
</tr>
<tr>
<td>Provides a score based on algorithmic measurement of 3 tumor factors:</td>
</tr>
<tr>
<td>• Loss of heterozygosity (LOH)</td>
</tr>
<tr>
<td>• Telomeric allelic imbalance (TAI)</td>
</tr>
<tr>
<td>• Large-scale state transitions (LST)</td>
</tr>
<tr>
<td>Homologous recombination status is determined by the following:</td>
</tr>
<tr>
<td>• HR-deficient tumors: Tissue test score ≥42 OR a BRCA mutation</td>
</tr>
<tr>
<td>• HR-proficient tumors: Tissue test score &lt;42</td>
</tr>
<tr>
<td>• HR-not-determined</td>
</tr>
</tbody>
</table>

HREC, homologous recombination deficient

**PRIMA enrollment and outcomes**

Median follow up of 13.8 months

- **733 randomized**
  - 370 HRd
  - 5 did not receive intervention
    - 3 HRd

- **728 received intervention**
  - 484 received niraparib
    - 245 HRd
    - 177 (37%) still receiving niraparib at data cutoff
      - 121 HRd
    - 124 HRd
      - 27 due to AE
      - 80 due to PD
      - 8 patient request

  - 244 received placebo
    - 125 HRd
    - 69 (28%) still receiving placebo at data cutoff
      - 42 HRd
    - 83 HRd
      - 2 due to AE
      - 76 due to PD
      - 0 patient request

  - 307 discontinued*
    - 58 due to AE
    - 218 due to PD (45%)
    - 12 patient request

*19 patients (8 HRd) and 7 patients (5 HRd) discontinued due to other reasons in the niraparib and placebo arms, respectively. AE, adverse event, HRd, homologous recombination deficient, PD, progression of disease.
### PRIMA patient characteristics and baseline demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Niraparib (n=487)</th>
<th>Placebo (n=246)</th>
<th>Overall (N=733)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>62 (32, 85)</td>
<td>62 (33, 88)</td>
<td>62 (32, 88)</td>
</tr>
<tr>
<td>Weight, median, kg</td>
<td>66</td>
<td>66</td>
<td>66</td>
</tr>
<tr>
<td>Stage at initial diagnosis, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>318 (65)</td>
<td>158 (64)</td>
<td>476 (65)</td>
</tr>
<tr>
<td>IV</td>
<td>169 (35)</td>
<td>88 (36)</td>
<td>257 (35)</td>
</tr>
<tr>
<td>Prior NACT, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>322 (66)</td>
<td>167 (68)</td>
<td>489 (67)</td>
</tr>
<tr>
<td>No</td>
<td>165 (34)</td>
<td>79 (32)</td>
<td>244 (33)</td>
</tr>
<tr>
<td>Best response to platinum-based CT, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>337 (69)</td>
<td>172 (70)</td>
<td>509 (69)</td>
</tr>
<tr>
<td>PR</td>
<td>150 (31)</td>
<td>74 (30)</td>
<td>224 (31)</td>
</tr>
<tr>
<td>Homologous recombination test status, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRd</td>
<td>247 (51)</td>
<td>126 (51)</td>
<td>373 (51)</td>
</tr>
<tr>
<td>BRCAmut</td>
<td>152 (31)</td>
<td>71 (29)</td>
<td>223 (30)</td>
</tr>
<tr>
<td>BRCAwt</td>
<td>95 (20)</td>
<td>55 (22)</td>
<td>150 (20)</td>
</tr>
<tr>
<td>HRp</td>
<td>169 (35)</td>
<td>80 (33)</td>
<td>249 (34)</td>
</tr>
<tr>
<td>HRnd</td>
<td>71 (15)</td>
<td>40 (16)</td>
<td>111 (15)</td>
</tr>
</tbody>
</table>

- 35% of patients were Stage IV
- 99.6% with Stage III had residual disease post PDS
- 67% received NACT
- 31% achieved a PR to 1L CT
- 51% had HRd tumors
- 30% had BRCAmut tumors
- 34% had HRp tumors

1L, first-line; CR, complete response; CT, chemotherapy; HRd, homologous recombination deficient; HRp, homologous recombination proficient; HRnd, homologous recombination not determined; mut, mutation; NACT, neoadjuvant chemotherapy; PR, partial response; wt, wild-type.
PRIMA primary endpoint, PFS benefit in the HR-deficient population

Hazard ratio: 0.43 (95% CI, 0.31–0.59)  
\(p<0.001\)

57% reduction in risk of relapse or death with niraparib

<table>
<thead>
<tr>
<th></th>
<th>Niraparib (n=247)</th>
<th>Placebo (n=126)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrogen</td>
<td>21.9</td>
<td>10.4</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(19.3–NE)</td>
<td>(8.1–12.1)</td>
</tr>
</tbody>
</table>

Patients without PD or death (%)

<table>
<thead>
<tr>
<th></th>
<th>6 months</th>
<th>12 months</th>
<th>18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrogen</td>
<td>86%</td>
<td>72%</td>
<td>59%</td>
</tr>
<tr>
<td>Placebo</td>
<td>68%</td>
<td>42%</td>
<td>35%</td>
</tr>
</tbody>
</table>

CI, confidence interval; NE, not estimable; PD, progressive disease; PFS, progression-free survival.

Sensitivity analysis of PFS by the investigator was similar to and supported the BICR analysis.
PRIMA primary endpoint, PFS benefit in the overall population

Hazard ratio: 0.62 (95% CI, 0.50–0.76)
p<0.001

38% reduction in risk of relapse or death with niraparib

<table>
<thead>
<tr>
<th></th>
<th>Niraparib (n=487)</th>
<th>Placebo (n=246)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS</td>
<td>13.8 (11.5–14.9)</td>
<td>8.2 (7.3–8.5)</td>
</tr>
<tr>
<td>Patients without PD or death (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>73%</td>
<td>60%</td>
</tr>
<tr>
<td>12 months</td>
<td>53%</td>
<td>35%</td>
</tr>
<tr>
<td>18 months</td>
<td>42%</td>
<td>28%</td>
</tr>
</tbody>
</table>

Initiation of PRIMA after completion of 1L CT

<table>
<thead>
<tr>
<th></th>
<th>Niraparib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>487</td>
<td>246</td>
</tr>
<tr>
<td>2</td>
<td>454</td>
<td>226</td>
</tr>
<tr>
<td>4</td>
<td>385</td>
<td>177</td>
</tr>
<tr>
<td>6</td>
<td>312</td>
<td>133</td>
</tr>
<tr>
<td>8</td>
<td>295</td>
<td>117</td>
</tr>
<tr>
<td>10</td>
<td>253</td>
<td>90</td>
</tr>
<tr>
<td>12</td>
<td>167</td>
<td>60</td>
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<tr>
<td>14</td>
<td>111</td>
<td>32</td>
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<tr>
<td>16</td>
<td>94</td>
<td>29</td>
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<td>18</td>
<td>58</td>
<td>17</td>
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<tr>
<td>20</td>
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<td>6</td>
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<tr>
<td>22</td>
<td>21</td>
<td>4</td>
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<td>24</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>26</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>28</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
PRIMA exploratory analysis, PFS benefit in pre-specified groups

<table>
<thead>
<tr>
<th>Homologus recombination status</th>
<th>HR for PFS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRd–BRCAmut</td>
<td>0.40 (0.27–0.62)</td>
</tr>
<tr>
<td>HRd–BRCAwt</td>
<td>0.50 (0.31–0.83)</td>
</tr>
<tr>
<td>HRp</td>
<td>0.68 (0.49–0.94)</td>
</tr>
<tr>
<td>HRnd</td>
<td>0.85 (0.51–1.43)</td>
</tr>
</tbody>
</table>

CI, confidence interval; CR, complete response; HRd, homologous recombination deficient; HRp, homologous recombination proficient; HRnd, homologous recombination not determined; mut, mutation; PFS, progression-free survival; PR, partial response; wt, wild-type
PRIMA PFS benefit in biomarker subgroups

Homologous Recombination Deficient (HRd)

• Niraparib provided similar clinical benefit in the HRd subgroups (BRCAmut and BCRAwt)
• Niraparib provide clinically significant benefit in the HR-proficient subgroup with a 32% risk reduction in progression or death
PRIMA key secondary endpoint, overall survival (11% data maturity)

Pre-planned interim analysis of overall survival numerically favors niraparib over placebo:
- overall population 84% vs 77% alive at 2 years
- HR-deficient 91% vs 85% alive at 2 years
- HR-proficient 81% vs 59% alive at 2 years
### PRIMA safety overview

<table>
<thead>
<tr>
<th>Adverse Event, no. (%)</th>
<th>Niraparib (n=484)</th>
<th>Placebo (n=244)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>478 (98.8)</td>
<td>224 (91.8)</td>
</tr>
<tr>
<td>Grade ≥3</td>
<td>341 (70.5)</td>
<td>46 (18.9)</td>
</tr>
<tr>
<td>Led to treatment discontinuation</td>
<td>58 (12.0)</td>
<td>6 (2.5)</td>
</tr>
<tr>
<td>Led to dose reduction</td>
<td>343 (70.9)</td>
<td>20 (8.2)</td>
</tr>
<tr>
<td>Led to dose interruption</td>
<td>385 (79.5)</td>
<td>44 (18.0)</td>
</tr>
<tr>
<td>TEAEs leading to death</td>
<td>2 (0.4)</td>
<td>1 (0.4)</td>
</tr>
</tbody>
</table>

- TEAEs were manageable and consistent with the PARP inhibitor class
- Dose interruptions were similar to those in the previous niraparib trials
- Treatment discontinuation due to thrombocytopenia was 4.3%
- TEAEs leading to death were determined to be not treatment-related
Available therapies and active surveillance do not address the high unmet need for many patients with newly diagnosed advanced ovarian cancer after platinum-based chemotherapy.

Niraparib therapy in patients with advanced ovarian cancer provided a clinically significantly improvement in PFS after response to 1L platinum-based chemotherapy in ALL patients.
  - PFS overall population: hazard ratio, 0.62; p<0.001
  - PFS homologous recombination deficient: hazard ratio, 0.43; p<0.001
  - PFS homologous recombination proficient: hazard ratio, 0.68; p=0.020

Niraparib is the first PARP-inhibitor to demonstrate benefit in patients across biomarkers subgroups after platinum-based chemotherapy in frontline, consistent with prior clinical studies of niraparib in recurrent ovarian cancer (NOVA and QUADRA).

Patients with ovarian cancer at the highest risk of early disease progression (NACT, partial responders to 1L platinum chemotherapy) had significant benefit with niraparib therapy.

- No new safety signals were observed, and quality of life was maintained on niraparib.
- Niraparib monotherapy after surgery and platinum-based chemotherapy could be an important new treatment option for patients.
Putting PRIMA in context

Dr Hal Barron, Chief Scientific Officer and President R&D
Why was Tesaro a smart risk?

1: Does Zejula offer a benefit to women with ovarian cancer with an HR deficiency (ie HRD positive) in the first line maintenance setting?

2: Does Zejula offer a benefit to all women with ovarian cancer in the first line maintenance setting?

The hypotheses:

- PARP inhibitors have efficacy beyond gBRCA patients and benefit patients with other forms of HR defect.
- Patients with HR proficient tumours (HRD-) benefit from an alternative mechanism including immune activation through the STING pathway or PDL1 upregulation, for which Zejula would be a uniquely suitable PARP inhibitor as it has unique pharmacokinetic properties.

Conclusions:

PRIMA met the primary endpoint with a highly statistically significant and clinically meaningful PFS improvement in both the HRD+ and all-comers populations.
Caution needs to be taken when making cross trial comparisons, especially when patient populations vary.

Hazard ratio better shows biological impact than mPFS

<table>
<thead>
<tr>
<th></th>
<th>PRIMA&lt;sup&gt;1&lt;/sup&gt; niraparib</th>
<th>SOLO-1&lt;sup&gt;2&lt;/sup&gt; olaparib</th>
<th>PAOLA-1&lt;sup&gt;3&lt;/sup&gt; bevacizumab +/- olaparib</th>
<th>VELIA&lt;sup&gt;4&lt;/sup&gt; veliparib</th>
<th>GOG-218&lt;sup&gt;5&lt;/sup&gt; bevacizumab</th>
<th>ICON7&lt;sup&gt;6&lt;/sup&gt; bevacizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>733</td>
<td>391</td>
<td>806</td>
<td>1140</td>
<td>1873</td>
<td>1528</td>
</tr>
<tr>
<td>Stage III: visible residual disease required after PDS</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Stage IV: inoperable disease</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>NACT permitted</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>BRCAmut only</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
</tr>
</tbody>
</table>

(N) BRCA mut only

(1) Gonzalez, ESMO 2019; (2) MORE, NEJM 2018; (3) Ray-Coquard ESMO 2019; Coleman ESMO 2019; (5) Burger NEJM 2011; (6) Perren NEJM 2011

PDS: primary debulking surgery; NACT: neoadjuvant chemotherapy
# Comparing PARPi and bevacizumab in 1L ovarian cancer

<table>
<thead>
<tr>
<th></th>
<th>PRIMA(^1) niraparib</th>
<th>SOLO-1(^2) olaparib</th>
<th>PAOLA-1(^3) bevacizumab +/− olaparib</th>
<th>VELIA(^4) veliparib</th>
<th>GOG-218(^5) bevacizumab</th>
<th>ICON7(^6) bevacizumab</th>
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\(\text{HR deficient BRCAmut} \sim \text{20\% of patients}\)

\(\text{HR deficient BRCAwt} \sim \text{30\% of patients}\)

\(\text{HR proficient BRCAwt} \sim \text{50\% of patients}\)

(1) Gonzalez, ESMO 2019; (2) MORE, NEJM 2018; (3) Ray-Coquard ESMO 2019; Coleman ESMO 2019; (5) Burger NEJM 2011; (6) Perren NEJM 2011

* Patients with known BRCA and HR status
## Comparing PARPi and bevacizumab in 1L ovarian cancer

### First conclusion

**Aggregate data demonstrate that HR deficient (HRD+) patients benefit from a PARPi**

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Comparing PARPi and bevacizumab in 1L ovarian cancer

Second conclusion

Bevacizumab demonstrated no benefit in HR deficient (HRD positive) patients

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Zejula is the only PARP inhibitor that demonstrated a benefit in HR proficient (HRD-) patients; bevacizumab showed a similar benefit

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Only Zejula demonstrated efficacy in all patient HR subgroups in first line

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* Patients with known BRCA and HR status
Could Zejula’s unique PK profile explain the benefit in HRD- patients?

At steady state, the concentration of niraparib is higher in the tumour than the plasma.

**BRCAnwt ovarian cancer model***

- **Tumor PK**
  - Niraparib (50 mg/kg qd 2 days)
  - Olaparib (67 mg/kg bid 2 days)

- **Plasma PK**
  - Niraparib (50 mg/kg qd 2 days)
  - Olaparib (67 mg/kg bid 2 days)

**BRCAmut TNBC model**

- MDA-MB-436 (BRCAtmut)
  - Vehicle (n=4)
  - Niraparib (75 mg/kg qd n=6)
  - Olaparib (75/67 mg/kg bid n=4)

**BRCAnwt ovarian model***

- A2780 (BRCAnwt)
  - Vehicle (n=15)
  - Niraparib (62.5 mg/kg qd n=6)
  - Olaparib (100 mg/kg qd n=6)

Kaiming Sun1, Keith Mikulec1, Zebin Wang1, Grace Poon1, Aparajitha Vaidyanathan2, Gillian Smith1, Zhi-Yi Zhang1, Jeffrey Hanke1, Sridhar Ramaswamy1 and Jing Wang1

“Our results show that at steady state, tumor exposure to niraparib is 3.3 times greater than plasma exposure in tumor xenograft mouse models. In comparison, the tumor exposure to olaparib is less than observed in plasma. In addition, niraparib crosses the blood-brain barrier and shows good sustainability in the brain, whereas sustained brain exposure to olaparib is not observed in the same models. Consistent with its favorable tumor and brain distribution, niraparib achieves more potent tumor growth inhibition than olaparib in BRCAnwt models and an intracranial tumor model at maximum tolerated doses (MTD).”

Sun et al

*OVC 134 PDX model; **MDA-MB-436 TNBC model; *** A2780 ovarian cancer model
Clinical confirmation of higher exposure to niraparib in tumour versus plasma in patients with breast cancer

Results provide the first data of the intra-tumour concentration of niraparib in the clinical setting.

Concentration of niraparib was ~36-fold greater in tumour tissue than in plasma.

Confirms preclinical data that showed that tumour concentration is higher than in plasma, a unique property of niraparib.

Efficacy results will be reported at a future meeting.
GSK Oncology: data at ESMO
ICOS: results from INDUCE-1

Axel Hoos, SVP Oncology R&D
# GSK Oncology: building on a strong foundation and investing for future performance

<table>
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<tr>
<th>Smart business development</th>
<th>Strong internal R&amp;D capabilities</th>
<th>Strengthening in market operations</th>
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<td>- Tesaro acquisition</td>
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<td>- Zejula expected to be</td>
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<td>build of infrastructure</td>
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<td>- Diverse portfolio of</td>
<td>- Focus on recruiting</td>
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- 17 assets in oncology pipeline
- 16 abstracts across 9 tumour types at ESMO
- Further important data expected at ASH’19 and ASCO’20
- 3 oncology filings expected by end 2019
Oncology R&D: strategy and scientific focus

Maximise patient survival through transformational medicines

- **Immuno-Oncology**
  - Advance IO to next gen IO medicines, agnostic to modalities

- **Cancer Epigenetics**
  - Establish epigenetic medicines for cancer

- **Oncology Cell Therapy**
  - Establish cell therapy for solid tumors

- **Synthetic Lethality**
  - Optimise use of PARP inhibitors and expand repertoire of synthetic lethal medicines

- **Experimental Medicine**
  - Clinical biomarker strategy
    - CDx
    - Collaborative networks
Data at ESMO: oncology clinical pipeline
Representing 8 clinical programs across four focus areas

Mechanism

Phase 1
(FTIH)

Phase 1
expansion / Phase 2

Phase 3
(pivotal)

PARP inhibitor (Zejula, niraparib)*
Anti-BCMA ADC (belantamab mafodotin, GSK ‘916)†
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First line maintenance ovarian, other solid tumors under investigation
Multiple myeloma
NSCLC, BTC, breast cancer, other solid tumors
Breast, prostate, other solid tumors and heme malignancies
Sarcoma, NSCLC, multiple myeloma
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Data at ESMO 2019
16 abstracts/presentations
3 presentations (2 oral, 1 discussion)

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† In-licensure or other partnership with third party
‡ Option based alliance with Immunocore Ltd. ImmTAC is a registered trademark of Immunocore Ltd.
* Being developed in a strategic global alliance between GSK and Merck KGaA, Darmstadt, Germany
^ Re-categorised from phase II to I following refinement of phase definitions
FTIH = first time in human; NSCLC = non small cell lung cancer; HNSCC = Head and neck squamous cell carcinoma; BTC = biliary tract cancer

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GSK’609 ICOS receptor agonist

Differentiated MOA with encouraging clinical data at ESMO 2019

Target

• ICOS, a member of the CD28 family of co-stimulatory receptors, has a pivotal role in the proliferation, differentiation, survival, and function of T cells
• Highly upregulated upon T-cell receptor stimulation and is expressed on tumour infiltrating lymphocytes in many tumours
• Consistent with CTLA-4 and PD-1 blockade, ICOS agonism is anticipated to modulate T-cell dynamics resulting in prolonged control of tumour growth kinetics and survival in patients

Agent

• Humanised IgG4 antibody selected for its potent binding, agonist activity through the human ICOS receptor and low/no T-cell depleting effects via antibody-dependent cellular toxicity
• Anti-tumour activity observed with an ICOS agonist is further enhanced in combination with CTLA-4 and PD-1 blockade in non-clinical models. ICOS agonist treatment led to upregulation of PD-1/PDL-1 expression in these models
• RNA-sequencing data shows strong correlation of ICOS and PD-L1 in solid tumours, further supporting clinical evaluation of this combination

Status

• Clinical activity observed with both monotherapy and PD-1 combination; HNSCC data presented at ESMO September 2019
• Pivotal studies in HNSCC to commence by early 2020
• Other studies ongoing including novel combinations across tumours


RRMM = Relapsed/Refractory malignant melanoma; RR HNSCC = Relapsed/Refractory Head and Neck Squamous Cell Carcinoma; NSCLC = non small cell lung cancer
ICOS: checkpoint modulation beyond PD-1
Association with successful IO mechanisms of action increases clinical PoS

Agonist receptor families

CTLA-4 and PD-1 Kinetics of Clinical Activity
Melanoma and Head & Neck Cancer

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<th>ORR</th>
<th>DOR</th>
<th>OS @ 2y</th>
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<td>Ipilimumab (CTLA-4) Melanoma 2L</td>
<td>11% (same as CTX)</td>
<td>&gt;2y</td>
<td>22%</td>
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<td>Pembrolizumab (PD-1) HNSCC 1L</td>
<td>17% vs 36% CTX</td>
<td>23mo vs 4mo</td>
<td>28% vs 17%</td>
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<td>Pembrolizumab (PD-1) + CTX HNSCC 1L</td>
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</table>

Low ORR, strong OS benefit relative to CTX

Mayes, Hance and Hoos, Nature Reviews Drug Discovery 2018

Hodi et al. NEJM 2010; Rischin et al., ASCO 2019
GSK’609: first time monotherapy activity has been seen with an ICOS agonist in multiple tumour types

Best tumour response HNSCC

Change from baseline in tumour measurement by dose level (irRECIST)

Monotherapy activity with durable response across multiple tumour types

irCR, immune-related complete response; irPD, immune-related progressive disease; irPR, immune-related partial response; irSD, immune-related stable disease; pembrolizumab ESMO 2019 poster: “Inducible T-cell co-stimulatory (ICOS) receptor agonist, GSK3359609, alone and in combination with pembrolizumab: preliminary results from INDUCE-1 expansion cohorts in head and neck squamous cell carcinoma (HNSCC)”
GSK’609: early data point to ORR of 24% in combination with pembrolizumab with durable responses

Durable response in combination cohort with all responding patients maintaining benefit for ≥6 months

Change from baseline in tumour measurement by dose level (irRECIST)

*Patients (non-randomised) from both DE and CE phases included; †patients received GSK3359609 0.3 mg + pembro 200 mg

ESMO 2019 poster: “Inducible T-cell co-stimulatory (ICOS) receptor agonist, GSK3359609, alone and in combination with pembrolizumab: preliminary results from INDUCE-1 expansion cohorts in head and neck squamous cell carcinoma (HNSCC)”
GSK’609: responses not correlated to PD-L1 expression suggesting ICOS agonist activity

A majority of patients with responses and stable disease have low PD1 expression supporting evidence of ICOS agonist activity

ESMO 2019 poster: "Inducible T-cell co-stimulatory (ICOS) receptor agonist, GSK3359609, alone and in combination with pembrolizumab: preliminary results from INDUCE-1 expansion cohorts in head and neck squamous cell carcinoma (HNSCC)"
GSK’609: safety and tolerability consistent with results previously reported

Monotherapy cohorts (Part 1A and 1B, N=22)

Combination cohort (Part 2A and 2B, N=58)

Treatment-related AEs in patients with HNSCC across all study cohorts in the monotherapy (n=22) and combination populations (n=58) were consistent with that previously reported.

ESMO 2019 poster: "Inducible T-cell co-stimulatory (ICOS) receptor agonist, GSK3359609, alone and in combination with pembrolizumab: preliminary results from INDUCE-1 expansion cohorts in head and neck squamous cell carcinoma (HNSCC)"
GSK’609: progressing to advanced trials and novel combinations

### Solid Tumours

**INDUCE-1**
- **POC**: Relapsed/refractory selected solid tumours
- **Study**: Open label dose escalation and expansion study of GSK’609 monotherapy and combination with pembrolizumab
- **Read-out**: 2016
- **N**: >500

**Study start**: Jan’19 2020

### HNSCC

**INDUCE-2**
- **POC**: Relapsed/ refractory HNSCC
- **Study**: Open label dose escalation and expansion study of GSK’609 in combination with tremelimumab
- **Read-out**: Dec’18
- **N**: 114

**INDUCE-3**
- **pivotal**: First line PD-1 positive recurrent or metastatic HNSCC
- **Study**: Randomised, double blind, adaptive study of GSK’609 or placebo in combination with pembrolizumab
- **Read-out**: End 2019
- **N**: 2023

**55k** patients*

### NSCLC

**ENTRÉE**
- **platform**: Relapsed/ refractory NSCLC
- **Study**: Open label platform study of novel regimens of GSK’609 mono and combo versus SoC
- **Read-out**: Jan’19
- **N**: 105

**130k** patients*

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* Drug-treated patients. Source: Kantar Patient Matrix for US, EU5 and Japan in 2019, September 2019

POC = proof of concept; HNSCC = head and neck squamous cell carcinoma; SoC = standard of care; NSCLC = non small cell lung cancer
Building our oncology commercial capabilities

Luke Miels, President Global Pharmaceuticals
**GSK Oncology: building on a strong foundation and investing for future performance**

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<th>Smart business development</th>
<th>Strong internal R&amp;D capabilities</th>
<th>Strengthening in market operations</th>
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<td>- Tesaro acquisition</td>
<td>- High calibre scientists within clinical teams</td>
<td>- Tesaro accelerated build of infrastructure</td>
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<td>- Zejula expected to be supported by PRIMA</td>
<td>- Diverse portfolio of potentially transformational medicines</td>
<td>- Focus on recruiting the best sales force and medical talent</td>
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<td>- Dostarlimab expected to file by end 2019</td>
<td>- Prioritisation and investment to accelerate promising assets including belantamab mafodotin, GSK’609</td>
<td>- Changed HCP engagement and sales rep incentivisation policies to be more competitive</td>
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<td>- Early stage IO pipeline</td>
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<td>- Merck KGaA global alliance on bintrafusp alfa (M7824)</td>
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17 assets in oncology pipeline

16 abstracts across 9 tumour types at ESMO

Further important data expected at ASH’19 and ASCO’20

3 oncology filings expected by end 2019

High calibre scientists within clinical teams

Diverse portfolio of potentially transformational medicines

Prioritisation and investment to accelerate promising assets including belantamab mafodotin, GSK’609

Tesaro accelerated build of infrastructure

Focus on recruiting the best sales force and medical talent

Changed HCP engagement and sales rep incentivisation policies to be more competitive

Strong internal R&D capabilities

Strengthening in market operations
Building our oncology commercial capability

**Improved engagement with HCPs**

Updated HCP engagement policies to improve how we help prescribers understand new data and clinical experience with our innovative products

**Attracting and retaining the best sales force talent**

Competitive sales force incentives for Specialty area in place to recruit, motivate and retain sales teams with the right levels of expertise and experience

**Seamless execution across functions and in markets**

Aligned efforts to ensure launch readiness for exciting oncology launches and drive value for patients and shareholders

**3 potential oncology launches in 2020**

Zejula 1L maintenance therapy (PRIMA) presented at ESMO 2019
- Significantly improved PFS in the overall population
- Filing expected by end 2019

Belantamab mafodotin (BCMA ADC) 4L Multiple Myeloma (DREAMM-2) to be presented at an upcoming medical congress
- Study met primary objective and demonstrated clinically meaningful ORR
- Filing expected by end 2019

Dostarlimab (PD-1) in recurrent endometrial cancer (GARNET) with interim data presented at SGO 2019
- Filing expected by end 2019
Expect increase in use of PARPs following ESMO data with 1L monotherapy taking leading share

PARPs underutilised in 1L and 2L ovarian cancer

Utilisation % of eligible maintenance patients (US)

- **2+L**
  - Watch & Wait: 31%
  - PARP: 45%
  - Bevacizumab: 37%
  - Non Platinum Chemo: 51%

- **1L**
  - Watch & Wait: 78%
  - PARP: 49%
  - Bevacizumab: 81%

Avastin combination presents challenges

- Combination of PARP + Avastin increases cost, toxicity and administration challenges in maintenance setting
- Avastin currently used in <20% of 1L maintenance ovarian cancer patients in US; <50% EU and Japan*
- May limit Avastin as option for 2L
- Avastin has not demonstrated overall survival benefit in 1L

Zejula uniquely positioned with PRIMA data

- Demonstrated benefit in all comers population including HRD negative patients
- Pre-planned interim analysis of overall survival numerically favours Zejula over placebo
- Unique PK properties with preclinical evidence suggesting greater tumour penetration*
- Oral, once daily monotherapy with low drug interactions – key in maintenance setting

*Flatiron Health data

**Watch and wait % changes ± 5% with variation in:
duration between last platinum administration date and sample end date
# of administered platinum cycles

*Sun et al, Oncotarget, 2018, Vol. 9, (No. 98), pp: 37080-37096
Dr Hal Barron

Hal joined GSK as Chief Scientific Officer and President, R&D on 1 January 2018. He is a member of the Board and the Corporate Executive Team.

His previous role was President, R&D at Calico (California Life Company). Prior to this, Hal was Executive Vice President, Head of Global Product Development, and Chief Medical Officer of Roche, responsible for all the products in the combined portfolio of Roche and Genentech. At Genentech, he was Senior Vice President of Development and Chief Medical Officer.

Hal was a Non-Executive Director and Chair of the Science & Technology Committee at Juno Therapeutics, Inc until March 2018, when it was acquired by Celgene Corporation. Hal is Associate Adjunct Professor, Epidemiology & Biostatistics, University of California, San Francisco. He is also a Non-Executive Board Director of GRAIL, Inc, an early cancer detection healthcare company and a member of the Advisory Board of Verily Life Sciences LLC, a subsidiary of Alphabet Inc.

Hal holds a Bachelor of Science degree in Physics from Washington University in St. Louis and a medical degree from Yale University. He completed his training in Cardiology and Internal Medicine at the University of California, San Francisco. He has been issued several patents for his work in thrombosis and angiogenesis and has published more than 90 papers in peer-reviewed scientific journals.
Dr. Antonio González-Martín graduated in medicine at University of Navarra in Pamplona, and subsequently trained in medical oncology at University Hospital Ramón y Cajal in Madrid from 1994 to 1997. During part of 1997 he attended as an observer to The Mount Sinai School of Medicine in New York. He joined as staff member of the Medical Oncology Service at University Hospital Ramón y Cajal in 1998. From January 2009 he gained the position of Head of Medical Oncology Department at MD Anderson Cancer Center Madrid, an affiliate institution of MD Anderson in Houston. He recently moved to Clinica Universidad de Navarra as head of Medical Oncology and co-director of the Oncology Department. He is Associate Professor at Medicine at Francisco de Vitoria University in Madrid and Adjunt Professor at University of Texas (TX, USA). He got the PhD degree at Francisco de Vitoria University in April 2018.

He specialises in the treatment of gynaecological and breast cancer and is the chairman of GEICO. He is also the representative of GEICO in ENGOT, and the current President of this Group. In addition, he is one of the representatives of GEICO in Gynecologic Cancer InterGroup, an international organisation for trials and treatment of gynaecological cancers, and by now is the chair of the ovarian cancer committee. He was also a member of the board of the Spanish Society of Medical Oncology, and member of GEICAM and SOLTI breast cancer cooperative groups.

He has several relevant publications in the field of gynaecological and breast cancer. He is considered an expert in ovarian and breast cancer and has lectured widely on these areas of interest.
Axel is SVP, R&D Governance Chair, and Therapeutic Area (TA) Head for Oncology at GSK, responsible for discovery and development in Oncology. As R&D governance chair he oversees technical and funding review committees. Axel also serves as Chairman of the Board of Trustees of the Sabin Vaccine Institute, a Global Health organization, Director on the Board of Imugene, a biotech company, Co-Director of the Cancer Immunotherapy Consortium and Scientific Advisory Board Member of the Cancer Research Institute. Through his leadership a paradigm for the development of cancer immunotherapies has been defined, which helped launch the field of Immuno-Oncology (Nat. Rev. Drug Discovery 2016, 15(4):, 235-47).

Previously, Axel was the Global Medical Lead in Immunology/Oncology at BMS where he developed Yervoy (Ipilimumab), the first life-extending therapy and the first checkpoint inhibitor drug in Immuno-Oncology. The discovery of ipilimumab’s scientific mechanism was honored with the Nobel prize for Physiology or Medicine to Dr. James Allison in 2018. Before BMS, Dr. Hoos was Senior Director of Clinical Development at Agenus Bio (previously Antigenics), a biotech company.

Dr. Hoos holds an MD from Ruprecht-Karls-University and a PhD in molecular oncology from the German Cancer Research Center (DKFZ) both in Heidelberg, Germany. He trained in surgery at the Technical University in Munich and further in surgery, molecular pathology and tumor immunology at Memorial Sloan-Kettering Cancer Center in New York City. He is an alumnus of the Program for Leadership Development at Harvard Business School.
Luke joined GSK as President, Global Pharmaceuticals in September 2017. He is a member of the Corporate Executive Team.

At GSK, he is responsible for commercialising a portfolio of medicines and vaccines with annual sales of more than £20 billion and operations in over 100 markets. His previous role was Executive Vice President of AstraZeneca’s European business and, prior to that, Executive Vice President of Global Product and Portfolio Strategy, Global Medical Affairs and Corporate Affairs.

Luke joined AstraZeneca from Roche, where he was Regional Vice President Asia Pacific for the Pharmaceuticals Division. Before then, he held roles of increasing seniority at Sanofi-Aventis in Asia and the US. He also co-led the US integration of Sanofi and Aventis. Prior to that, he held general management roles in Thailand and New Zealand, following his entry into the industry in Australia.

He holds a Bachelor of Science degree in Biology from Flinders University in Adelaide and an MBA from the Macquarie University, Sydney.
Christine Roth

Christine re-joined GSK as SVP, Global Oncology Therapy Area Head in December 2017, reporting to Luke Miels. As the global commercial lead for oncology, Christine is a member of the Pharmaceutical Leadership Team, Forecast Review Committee, Research Investment Board, Development Review Board, and Global Pharmaceutical Leadership Team.

After beginning her career as a scientist, Christine joined BMS and progressed through commercial leadership roles in multiple therapeutic and functional areas. Together with Axel Hoos, she was a pioneer in Immuno-Oncology, serving as the commercial lead for the first approved I-O therapy, Yervoy (ipilimumab) and working on BMS’s String of Pearls strategy which led to the acquisition of Medarex and the first PD-1, Opdivo.

Christine was delighted to return to GSK and partner again with Axel and the GSK Oncology team to build a new and improved, world-class oncology organization.
Jenn Christensen

Jennifer completed her masters degree in Organic Chemistry from Brandeis University, Massachusetts. She has worked at a number of biotech companies including Tesaro, Xanthus/ Antisoma and Datide Research Laboratories.

Jennifer joined Tesaro in 2011 to initially lead the Varubi programme and is currently the medical development lead for Zejula (niraparib) in ovarian cancer.
Marc S Ballas, MD, MPH is an Albert Einstein School of Medicine trained physician who completed his medical oncology/hematology at NIH and practiced as Assistant Professor at NYU Langone School of Medicine before joining the pharmaceutical industry.

Early on, he has been involved in the immune-oncology field working on late stage development of ipilimumab in small cell lung cancer, durvalumab in locally advanced and adjuvant non-small cell lung cancer.

Marc is currently the medical development lead for the GSK’609 ICOS agonist across solid tumors.