54th ASCO Annual Meeting, Chicago

Roche Analyst Event
Monday, 4 June 2018
Agenda

Welcome
Karl Mahler, Head of Investor Relations

Highlights in cancer immunotherapy
Alan Sandler, Global Head Lung Cancer Franchise

Biomarkers in the era of cancer immunotherapy
Priti S. Hegde, Ph.D., Oncology Biomarker Development

Highlights late stage portfolio outside cancer immunotherapy
Sandra Horning, M.D., Chief Medical Officer and Head Global Product Development

Oncology strategy update
Daniel O’Day, CEO Roche Pharmaceuticals

Q&A
Welcome

Karl Mahler
Head of Investor Relations
1L non-sq NSCLC evolving options

Non-Squamous

<table>
<thead>
<tr>
<th>PD-L1 status</th>
<th>Negative (TPS&lt;1%) (~5%)</th>
<th>Low (TPS=1-4%) (~20%)</th>
<th>High (TPS=50-80%) (~25%)</th>
</tr>
</thead>
</table>

Illustrative

✓ = Positive data

Pembrolizumab monotherapy

KN-024

Status ASCO 2016
Crowded news flow in the CIT lung cancer space

Key trial readouts highlighted
# 1L non-sq NSCLC evolving options - Complexity increases

## Non-Squamous

<table>
<thead>
<tr>
<th>EGFR/ALK+ liver metastases</th>
<th>EGFR/ALK negative or unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tecentriq + Avastin + carbo + pac</strong></td>
<td><strong>aPD-(L)1 + pemetrexed + platinum</strong></td>
</tr>
<tr>
<td>IMpower150</td>
<td>KN–189</td>
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<tr>
<td>KN–189</td>
<td>IMpower132</td>
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<tr>
<td>IMpower130</td>
<td></td>
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<tr>
<td>CM-227 (TMB)</td>
<td>MYSTIC (PDL1+ OS)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PD-L1 status</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>High</strong> (TPS25–50%) (~25%)</td>
<td><strong>Pembrolizumab monotherapy</strong></td>
</tr>
<tr>
<td>KN–024 and KN–042</td>
<td></td>
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</table>

**Illustrative**

✓ = Positive data

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Status ASCO 2018
Highlights in cancer immunotherapy

Alan Sandler, M.D.
Global Head Lung Cancer Franchise
IMpower150: Tecentriq + chemo ± Avastin in 1L non-sq NSCLC

IMpower131: Tecentriq + chemo in 1L sq NSCLC

GO30140: Tecentriq + Avastin in 1L HCC
**IMpower150 study design**

**Study design**

Stage IV or recurrent metastatic non-squamous NSCLC chemotherapy-naïve\(^a\)
any PD-L1 IHC
N = 1202

- **Arm A**: TECENTRIQ\(^b\) + CP
- **Arm B**: TECENTRIQ + CP + Avastin\(^e\)
- **Arm C**: (control) Avastin

**Co-primary endpoints Arm B vs C**
- Investigator-assessed PFS,OS (ITT)
- INV-assessed PFS in Teff-high WT

**Maintenance therapy** (no crossover permitted) until PD or loss of clinical benefit

**Survival follow-up**

**Statistical testing hierarchy**

- **Positive PFS Nov 2017, presented at ESMO IO**
  - PFS in ITT-WT, Teff-high WT
  - OS in ITT-WT

- **Positive OS Mar 2018, presented at ASCO**
  - Once OS is mature
  - Arm A vs Arm C
    - A vs C only tested if OS for B vs C is statistically significant

---

\(^a\) Patients with a sensitizing EGFR mutation or ALK translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies.

\(^b\) Tecentriq: 1200 mg IV q3w. CP carboplatin: AUC 6 IV q3w; paclitaxel: 200 mg/m\(^2\) IV q3w. Bevacizumab: 15 mg/kg IV q3w. ITT-WT refers to patients without EGFR or ALK genetic alterations.
Combination with Avastin

*Increased T cell infiltration and clinical activity*

On-treatment biopsies show increased infiltrate and reduction in tumor vasculature

**CD8**
- Pre-treatment
- Avastin
- Avastin + aPD-L1

**CD31**
- Pre-treatment
- Avastin
- Avastin + aPD-L1

E4599 in 1L NSCLC: OS benefit with Avastin + CP versus CP

Understanding the immune modulatory properties of a-VEGF have guided the regimens for IMpower150, IMmotion151 and IMbrave150

Sznol et al. ASCO GU 2015; Sandler A et al. N Engl J Med 2006;355:2542-2550; IMpower150, IMmotion151, IMbrave150 refer to ongoing Ph3 studies in 1L NSCLC, 1L RCC, 1L HCC

CP = carboplatin
IMpower150: Co-primary PFS and OS endpoints met in ITT-WT (Arm B vs C)

PFS for Tecentriq + Avastin + chemo improved with additional follow-up

- **Median, 8.3 mo** (95% CI: 7.7, 9.8)
- **HR**: 0.59 (95% CI: 0.50, 0.70)
- **P**: <0.0001

Statistically significant and clinically meaningful OS for Tecentriq + Avastin + chemo vs Avastin + chemo

- **Median, 14.7 mo** (95% CI: 13.3, 16.9)
- **HR**: 0.78 (95% CI: 0.64, 0.96)
- **P**: 0.0164

Arm A vs C: Positive trend toward OS benefit with Tecentriq + chemo vs Avastin + chemo; final OS analysis expected in 2019

**PFS for Tecentriq + Avastin + chemo**

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Arm B: Atezo+Bev+CP</th>
<th>Arm C: Bev+CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Median, 8.3 mo</td>
<td>Median, 6.8 mo</td>
</tr>
<tr>
<td></td>
<td>(95% CI: 7.7, 9.8)</td>
<td>(95% CI: 6.0, 7.1)</td>
</tr>
</tbody>
</table>

**Landmark PFS, %**

<table>
<thead>
<tr>
<th></th>
<th>Arm B</th>
<th>Arm C</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-month</td>
<td>38%</td>
<td>20%</td>
</tr>
<tr>
<td>18-month</td>
<td>27%</td>
<td>8%</td>
</tr>
</tbody>
</table>

**Overall Survival (%)**

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Arm B: Atezo+Bev+CP</th>
<th>Arm C: Bev+CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median follow-up ~20 months</td>
<td>Median, 19.2 mo (95% CI: 17.0, 23.8)</td>
<td>Median, 14.7 mo (95% CI: 13.3, 16.9)</td>
</tr>
</tbody>
</table>

**Landmark OS, %**

<table>
<thead>
<tr>
<th></th>
<th>Arm B</th>
<th>Arm C</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-month</td>
<td>43%</td>
<td>34%</td>
</tr>
</tbody>
</table>

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*a* Stratified HR. *b* For descriptive purposes only. Data cutoff: January 22, 2018. Minimum follow-up: 13.5 months
### Meaningful OS in key subgroups (Arm B vs C)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Median OS, mo&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Hazard Ratio&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arm B</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-L1–High (TC3 or IC3) WT</td>
<td>136 (20%)</td>
<td>25.2</td>
<td>0.70</td>
</tr>
<tr>
<td>PD-L1–Low (TC1/2 or IC1/2)&lt;sup&gt;b&lt;/sup&gt; WT</td>
<td>226 (32%)</td>
<td>20.3</td>
<td>0.80</td>
</tr>
<tr>
<td>PD-L1–Negative (TC0 and IC0) WT</td>
<td>339 (49%)</td>
<td>17.1</td>
<td>0.82</td>
</tr>
<tr>
<td>Liver Metastases WT</td>
<td>94 (14%)</td>
<td>13.2</td>
<td>0.54</td>
</tr>
<tr>
<td>No Liver Metastases WT</td>
<td>602 (86%)</td>
<td>19.8</td>
<td>0.83</td>
</tr>
<tr>
<td>ITT (including EGFR/ALK+)</td>
<td>800 (100%)</td>
<td>19.8</td>
<td>0.76</td>
</tr>
<tr>
<td>EGFR/ALK+ only&lt;sup&gt;c&lt;/sup&gt;</td>
<td>104 (13%)</td>
<td>NE</td>
<td>0.54</td>
</tr>
<tr>
<td><strong>Arm C</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD-L1–High (TC3 or IC3) WT</td>
<td>136 (20%)</td>
<td>15.0</td>
<td></td>
</tr>
<tr>
<td>PD-L1–Low (TC1/2 or IC1/2)&lt;sup&gt;b&lt;/sup&gt; WT</td>
<td>226 (32%)</td>
<td>16.4</td>
<td></td>
</tr>
<tr>
<td>PD-L1–Negative (TC0 and IC0) WT</td>
<td>339 (49%)</td>
<td>14.1</td>
<td></td>
</tr>
</tbody>
</table>

**OS benefit with Tecentriq + Avastin + chemo observed across all subgroups, including patients with sensitizing EGFR or ALK genomic rearrangements, liver metastases at baseline and PD-L1 expression subgroups**

<sup>a</sup> Prevalence % for PD-L1 IHC and liver metastases subgroups out of ITT-WT (n=696); prevalence of ITT, EGFR/ALK+, and ITT-WT out of ITT (n=800). <sup>b</sup> Mutually exclusive subgroup that excludes TC3 or IC3 patients from the TC1/2/3 or IC1/2/3 subgroup. <sup>c</sup> Patients with a sensitizing EGFR mutation or ALK translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. <sup>d</sup> Stratified HR for ITT-WT; unstratified HR for all other subgroups. Data cutoff: January 22, 2018
Addition of Avastin to Tecentriq and chemo prolongs survival of EGFR/ALK+ patients

Addition of Avastin to Tecentriq and chemo led to clinical benefit in patients with EGFR/ALK genomic alterations supporting previous reports of Avastin efficacy in these patients.

Arm B vs Arm C

HR\(^a\), 0.54
(95% CI: 0.29, 1.03)

Arm A vs Arm C

HR\(^a\), 0.82
(95% CI: 0.49, 1.37)

Data cutoff: January 22, 2018

\(^a\) Unstratified HR. \(^b\) Patients with a sensitizing EGFR mutation or ALK translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. \(^1\) Seto T, et al. Lancet Oncol, 2014. 2. Sandler A, et al. N Engl J Med, 2006
Addition of Avastin to Tecentriq and chemo prolongs survival of patients with liver metastases

Adding Avastin to Tecentriq and chemo led to clinical benefit in patients with liver metastases supporting previous reports of Avastin efficacy in these patients.

Data cutoff: January 22, 2018

a Unstratified HR. b Patients with a sensitizing EGFR mutation or ALK translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. 1 Sandler A et al. N Engl J Med 2006;355:2542-2550
IMpower150 conclusions

• Co-primary PFS and OS endpoints met with a statistically significant and clinically meaningful PFS and OS benefit for Tecentriq + Avastin + chemo (Arm B) vs Avastin + chemo (Arm C) in 1L non-squamous NSCLC

• OS benefit with Tecentriq + Avastin + chemo observed across all subgroups, including PD-L1 expression subgroups, patients with sensitizing EGFR or ALK genomic rearrangements, and patients with liver metastases at baseline
  – Supports previous reports of Avastin efficacy in these patient populations1,2

• Tecentriq in combination with chemo ± Avastin continued to be well tolerated and its safety profile was consistent with the known safety risks of the individual therapies

Tecentriq + Avastin + chemo combination provides a new treatment option for key patient populations with EGFR or ALK genomic rearrangements, and liver metastases

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IMpower150: Tecentriq + chemo ± Avastin in 1L non-sq NSCLC

IMpower131: Tecentriq + chemo in 1L sq NSCLC

GO30140: Tecentriq + Avastin in 1L HCC
IMpower131 study design

**Study design**

Stage IV squamous NSCLC chemotherapy-naïve<sup>a</sup>
ECOG PS 0–1
N = 1021

<table>
<thead>
<tr>
<th>Arm A</th>
<th>Arm B</th>
<th>Arm C</th>
</tr>
</thead>
<tbody>
<tr>
<td>TECENTRIQ&lt;sup&gt;b&lt;/sup&gt; + CP</td>
<td>TECENTRIQ + carbo + nab-P</td>
<td>(control) carbo + nab-P</td>
</tr>
</tbody>
</table>

Maintenance therapy with Tecentriq or BSC (no crossover permitted) until PD or loss of clinical benefit

**Survival follow-up**

Co-primary endpoints Arm B vs C
- Investigator-assessed PFS (ITT)
- OS (ITT)

**Statistical testing hierarchy**

Positive OS Mar 2018, presented at ASCO

- Arm B vs Arm C
  - PFS in ITT-WT
  - OS in ITT-WT

- Arm A vs Arm C
  - A vs C only tested if OS for B vs C is statistically significant
  - PFS in ITT-WT
  - OS in ITT-WT

<sup>a</sup>ITT population includes patients with EGFR mutations and ALK translocations; patients with a sensitizing EGFR mutation or ALK translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies.

<sup>b</sup>Tecentriq: 1200 mg IV q3w.
<sup>c</sup>CP: carboplatin AUC 6 IV q3w; paclitaxel 200 mg/m2 IV q3w.
<sup>d</sup>nab-P: nab-paclitaxel 100 mg/m2 IV qw
**PFS and subgroups in ITT (Arm B vs Arm C)**

**INV-assessed PFS - ITT**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Median PFS (95% CI), mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezo+CnP</td>
<td>6.3 (5.7, 7.1)</td>
</tr>
<tr>
<td>CnP</td>
<td>5.6 (5.5, 5.7)</td>
</tr>
</tbody>
</table>

- HR\(^a\), 0.71 (95% CI: 0.60, 0.85) \(p<0.0001\)

**12-month PFS**

- 24.7%
- 12.0%

- Minimum follow-up: 9.8 mo; median follow-up: 17.1 mo

**INV-assessed PFS in PD-L1 subgroups**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n (%)</th>
<th>Median PFS, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1 Positive (TC1/2/3 or IC1/2/3)</td>
<td>351 (52)</td>
<td>Arm B: 7.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm C: 5.6</td>
</tr>
<tr>
<td>PD-L1 High (TC3 or IC3)</td>
<td>101 (15)</td>
<td>Arm B: 10.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm C: 5.5</td>
</tr>
<tr>
<td>PD-L1 Low (TC1/2 or IC1/2)</td>
<td>250 (37)</td>
<td>Arm B: 6.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm C: 5.6</td>
</tr>
<tr>
<td>PD-L1 Negative (TC0 and IC0)</td>
<td>331 (48)</td>
<td>Arm B: 5.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arm C: 5.6</td>
</tr>
</tbody>
</table>

**ITT Population**

| 683 (100) |

**PFS benefit with Tecentriq + CnP (Arm B) vs CnP (Arm C) observed across all PD-L1–expressing subgroups, enriched with higher PD-L1 expression**

Data cutoff: January 22, 2018,

* Unstratified HR; unstratified HRs for all PD-L1 subgroups. INV=investigator; CnP = carboplatin + nab-paclitaxel
IMpower131: First interim OS in ITT (Arm B vs Arm C)

Arm B:
Atezo+CnP
Arm C:
CnP

Median OS (95% CI), mo:
Arm B: 14.0 (12.0, 17.0)
Arm C: 13.9 (12.3, 16.4)

HR (95% CI):
Arm B: 0.96 (0.78, 1.18)
Arm C: 0.6931

P value:
Arm B: 0.96 (0.78, 1.18)
Arm C: 0.6931

Next interim OS analysis anticipated in H2 2018

Data cutoff: January 22, 2018
* Unstratified HR, CNP = carboplatin + nab-paclitaxel
IMpower131 summary

- Study met co-primary endpoint of investigator-assessed PFS in Arm B vs Arm C in the ITT population
- PFS benefit with Tecentriq + CnP (Arm B) vs CnP (Arm C) was observed across all PD-L1-expressing subgroups, and was enriched in subgroups with higher PD-L1 expression
- Tecentriq + CnP median PFS in-line with other CIT + chemo combinations
- ORR numerically improved with enrichment by PD-L1 status
- OS benefit not significant at this time, with high cross-over to subsequent immunotherapy observed (42%). OS continues to be followed, with the next interim OS analysis anticipated later in 2018
- Tecentriq plus carboplatin and nab-paclitaxel has a manageable safety profile consistent with known safety risks of the individual therapies; no new safety signals were identified

CnP = carboplatin + nab-paclitaxel
Evolving landscape in 1L NSCLC
*Treatment driven by histology and actionable mutations*

<table>
<thead>
<tr>
<th></th>
<th>Non-Squamous</th>
<th>Squamous</th>
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<tbody>
<tr>
<td><strong>EGFR/ALK+</strong></td>
<td>EGFR/ALK negative or unknown</td>
<td></td>
</tr>
<tr>
<td>PD-L1</td>
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<td></td>
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<td>MYSTIC (PDL1+ OS)</td>
</tr>
<tr>
<td></td>
<td>KN-189</td>
<td>KN-407</td>
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<tr>
<td></td>
<td>IMpower130</td>
<td>IMpower131</td>
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<tr>
<td></td>
<td>CM-227 (TMB)</td>
<td></td>
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</tbody>
</table>

Illustrative ✔️ = Positive Roche data

Monotherapy: KN-24 and KN-42
Broad portfolio in NSCLC today and looking ahead

*Ability to cover all key segments*

<table>
<thead>
<tr>
<th>ALK</th>
<th>EGFR</th>
<th>RET</th>
<th>ROS</th>
<th>NTRK</th>
<th>Non-Driver</th>
<th>NSCLC (NSq)</th>
<th>NSCLC (Sq)</th>
<th>SCLC</th>
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<tr>
<td>Neo-/-Adj</td>
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<tr>
<td>1L</td>
<td>Alecensa</td>
<td>Tarceva ± Avastin</td>
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<td>IMpower010 (adj)</td>
<td>IMpower030 (neoadj)</td>
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<tr>
<td>IMpower110</td>
<td>Tecentriq</td>
<td>Tecentriq + platinum-based chemo</td>
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</tr>
<tr>
<td>IMpower150</td>
<td>Tecentriq + Avastin + CP</td>
<td>IMpower130</td>
<td>IMpower132</td>
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<tr>
<td>IMpower131</td>
<td>Tecentriq + CnP</td>
<td>IMpower110</td>
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<tr>
<td>IMpower133</td>
<td>Tecentriq + carboplatin + etoposide</td>
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</tr>
<tr>
<td>2L</td>
<td>IMpower150</td>
<td>Tarceva ± Avastin + CP</td>
<td></td>
<td></td>
<td>OAK, POPLAR, BIRCH</td>
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<tr>
<td>IMpower110</td>
<td>Tecentriq</td>
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<tr>
<td>Tarceva</td>
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</table>
IMpower150: Tecentriq + chemo ± Avastin in 1L non-sq NSCLC

IMpower131: Tecentriq + chemo in 1L sq NSCLC

GO30140: Tecentriq + Avastin in 1L HCC
Tecentriq + Avastin in 1L hepatocellular carcinoma
Encouraging phase 1 data, phase 3 study ongoing

- The combination of Tecentriq and Avastin shows promising early efficacy in patients with advanced HCC
- Confirmed ORR by RECIST v1.1 of 61% by INV; 10/14 responses are ongoing >6 months with 3 responses ongoing >12 months
- Median OS, PFS, and DOR have not yet been reached
- Combination of Tecentriq and Avastin was safe and well tolerated, no new safety signals
- Phase 3 (IMbrave150) of Tecentriq+Avastin vs. sorafenib ongoing

*minimum follow-up 16 weeks, median follow-up 10.3 months, evaluable patients (n=23)
Biomarkers in the era of cancer immunotherapy

Priti S. Hegde, Ph.D.
Director, Oncology Biomarker Development
Scientific inquiry to identify increasingly effective & meaningful biomarkers that are predictive of patient response

Incorporate science and biomarker findings into studies to develop best CIT regimen for each patient

Develop and commercialize diagnostic tests to identify patients for best therapy

Clinical Research

Science

Biomarkers

Diagnostics

Clinical Practice

Helps understand immune response and resistance

Inform rational clinical trial design

Inform patient identification
Scientific understanding to identify combinations
Establishing treatment options tailored to the specific immune biology associated with a tumor type

Understanding the immune modulatory properties of aVEGF has guided the regimens for IMpower150, IMmotion151 and IMbrave150

Dx leadership in an increasingly fragmented treatment landscape

Moving from AC trials to disease-specific Dx subsets

**PD-L1 IHC**
- In the front-line setting, PD-L1 performs well in enriching for patients with PFS benefit (50-55% of the patient population)

**T\(_{\text{eff}}\) gene signature**
- T\(_{\text{eff}}\) gene signature is equivalent to PD-L1 IHC

**TMB**
- Response rate and duration of response to CPI correlate with TMB levels across different tumor types
- TMB identifies a distinct patient population not currently captured by PD-L1 IHC

**NGS testing**
- NGS testing for rare biomarkers and as a standard test across tumor types

AC=all comers; Dx=diagnostic; TMB=tumor mutational burden; IHC=immunohistochemistry; NGS=next generation sequencing; CPI=checkpoint inhibitor
PD-L1 IHC assays are clinically equivalent. IMpower150 demonstrates high concordance between SP142 and SP263.

**PD-L1 IHC prevalence**

<table>
<thead>
<tr>
<th></th>
<th>SP142</th>
<th>SP263</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence (%)</td>
<td>47%</td>
<td>47%</td>
</tr>
<tr>
<td>Low (TC1/2 or I1/2)</td>
<td>33%</td>
<td>28%</td>
</tr>
<tr>
<td>High (TC3 or IC3)</td>
<td>20%</td>
<td>25%</td>
</tr>
</tbody>
</table>

**Similar PFS HRs across PD-L1 subgroups**

- **SP142**
  - TC1/2 or IC1/2
  - Arm B: aezo + bev + CP
  - Arm C: bev + CP
  - HR*: 0.53 (95% CI: 0.37, 0.76)

- **SP263**
  - 50% > TC ≥ 1%
  - Arm B: aezo + bev + CP
  - Arm C: bev + CP
  - HR*: 0.57 (95% CI: 0.38, 0.84)

**PFS Analysis in BEP of Arms B and C in ITT-WT (n=503)**

Kowanetz M et al., AACR 2018

*Unstratified HR. †Prevalence analysis of Arms B and C in the BEP (evaluable for SP263), n=503. TC3 or IC3=PD-L1+ ≥50% of TC or ≥10% of IC; TC1/2 or IC1/2=PD-L1+ <50% and ≥1% of TC or <10% and ≥1% of IC; TC0 and IC0=PD-L1+ <1% of TC and IC. Data cutoff: September 15, 2017.

BEP=biomarker evaluable population; IC=tumor-infiltrating immune cells; TC=tumor cells; bev=bevacizumab; CP=carboplatin+paclitaxel
Complex biology behind efficacy of immune checkpoint inhibitors
Capturing factors in addition to PD-L1 expression


TMB=tumor mutational burden; MSI=microsatellite instability; IHC=immunohistochemistry; NGS=next generation sequencing

Robust biomarker research might allow to personalize cancer immunotherapy for patients in the future
High tissue-based TMB (tTMB) is associated with enriched ORR and DOR across tumor types and lines of therapy

TMB cutoffs shown are measured in mut/Mb (date of analysis: November 1, 2017); *Balar AV et al., Lancet. 2017 Jan 7;389(10064):67-76. tTMB was evaluated by the FoundationOne (F1) assay across 7 Tecentriq monotherapy studies: NSCLC n=342 (FIR, BIRCH, POPLAR, OAK), metastatic urothelial carcinoma (mUC) n=400 (IMvigor210, 211), and other advanced solid tumors n=245 (PCD4989g). ORR=objective response rate; DOR=duration of response; tTMB=tissue-based tumor mutational burden; BEP=biomarker evaluable population; NR=not reached

Objective Response Rate

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>n (%)</th>
<th>ORR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled BEP</td>
<td>987 (100%)</td>
<td>16% (14, 19)</td>
</tr>
<tr>
<td>TMB ≥ 4</td>
<td>815 (83%)</td>
<td>18% (15, 20)</td>
</tr>
<tr>
<td>TMB ≥ 10</td>
<td>387 (39%)</td>
<td>24% (20, 28)</td>
</tr>
<tr>
<td>TMB ≥ 16</td>
<td>175 (18%)</td>
<td>30% (23, 37)</td>
</tr>
<tr>
<td>TMB ≥ 20</td>
<td>119 (12%)</td>
<td>33% (24, 42)</td>
</tr>
<tr>
<td>TMB ≥ 24</td>
<td>80 (8%)</td>
<td>36% (26, 48)</td>
</tr>
<tr>
<td>TMB ≥ 26</td>
<td>66 (7%)</td>
<td>39% (28, 52)</td>
</tr>
</tbody>
</table>

ORR by tTMB cut-offs

ORR and DOR in tTMB* ≥16 vs <16 subgroups

Results are encouraging in the understanding of the mechanisms underlying responses to cancer immunotherapy

Legrand FA et al., ASCO 2018
Oral presentation on Tuesday, Jun 5th

Legrand FA et al., ASCO 2018

TMB cutoffs shown are measured in mut/Mb (date of analysis: November 1, 2017); *Balar AV et al., Lancet. 2017 Jan 7;389(10064):67-76. tTMB was evaluated by the FoundationOne (F1) assay across 7 Tecentriq monotherapy studies: NSCLC n=342 (FIR, BIRCH, POPLAR, OAK), metastatic urothelial carcinoma (mUC) n=400 (IMvigor210, 211), and other advanced solid tumors n=245 (PCD4989g). ORR=objective response rate; DOR=duration of response; tTMB=tissue-based tumor mutational burden; BEP=biomarker evaluable population; NR=not reached
Blood-based TMB (bTMB): A non-invasive biomarker

~30% of patients with NSCLC have inadequate tumor tissue for molecular testing

OAK Ph3: bTMB ≥16 predicts PFS benefit

- bTMB ≥16
- PD-L1 TC3 or IC3

n=156
n=30
n=73

PFS HR (95% CI) | OS HR (95% CI)
---|---
bTMB ≥16 | 0.64 (0.46, 0.91) | 0.64 (0.44, 0.93)
TC3 or IC3 | 0.62 (0.41, 0.93) | 0.44 (0.27, 0.71)
bTMB ≥16 and TC3 or IC3 | 0.38 (0.17, 0.85) | 0.23 (0.09, 0.58)

B-F1RST Ph2: Prospective evaluation of bTMB

- Fully enrolled
- Patients with stage IIIB/IVB advanced or metastatic NSCLC (any histology)
- Tecentriq 1200 mg IV q3w
- Until PD, loss of clinical benefit or unacceptable toxicity

Interim Analysis: Prespecified at 6 mo after 50% of patients have been enrolled
Primary analysis: ORR and PFS (co-primary endpoints), expected later in 2018

bTMB identified patients who derived greater PFS benefit from Tecentriq as compared to the all-comer population in the two original NSCLC studies (POPLAR and OAK)

1Rittmeyer A et al., Lancet, 2017; 2Gandara DR et al., ESMO 2017; 3The bTMB assay uses hybridization-capture methodology and targets 1.1 Mb of genomic coding sequence (bTMB score of 16 = 14 mutations/Mb). 4PD-L1 expression on ≥50% of tumor cells or ≥10% of immune cells
bTMB=blood-based tumor mutational burden; CPI=checkpoint inhibitor; BEP=biomarker evaluable population; IC=tumor-infiltrating immune cells; TC=tumor cells; ORR=objective response rate
B-F1RST: bTMB enriches for PFS benefit of Tecentriq in 1L NSCLC
A potentially clinically relevant biomarker to inform treatment strategies

Interim analysis results support the bTMB selection of patients in the ongoing, label-enabling Ph3 BFAST study

<table>
<thead>
<tr>
<th>RECIST v1.1</th>
<th>IAP (n = 78)</th>
<th>BEP (n = 58)</th>
<th>bTMB low (n = 47)</th>
<th>bTMB high (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>15.4%</td>
<td>12.1%</td>
<td>6.4%</td>
<td>36.4%</td>
</tr>
<tr>
<td>PR</td>
<td>15.4%</td>
<td>12.1%</td>
<td>6.4%</td>
<td>36.4%</td>
</tr>
<tr>
<td>SD</td>
<td>33.3%</td>
<td>34.5%</td>
<td>36.2%</td>
<td>27.3%</td>
</tr>
<tr>
<td>PD</td>
<td>37.2%</td>
<td>37.9%</td>
<td>38.3%</td>
<td>36.4%</td>
</tr>
</tbody>
</table>

Minimum follow-up: 6 months

Velchetti V et al., ASCO 2018
Oral presentation on Tuesday, Jun 5th

- Per protocol, efficacy differences between bTMB high vs low subgroups are tested at a significance level of 0.1, and 90% CIs are provided. Unconfirmed ORR (2 patients had only 1 scan prior to clinical cut-off).
- bTMB high, ≥16; bTMB low, <16. BEP comprised patients with a baseline evaluable blood sample with adequate tumor content (i.e. maximum somatic allele frequency [MSAF] ≥1%) to test on the FMI bTMB assay. IAP=interim analysis population; BEP=biomarker-evaluable population; bTMB=blood-based TMB; ORR=objective response rate; PR=partial response; SD=stable disease; PD=progressive disease
| **PD-L1 IHC** | • Increasing PFS benefit associated with higher PD-L1 expression (IMmotion151)  
• Increasing OS benefit associated with higher PD-L1 expression (OAK, IMpower150)  
• SP142 and 22c3/SP263 are interchangeable (OAK, IMpower150) |
| **T_{\text{eff}}$$ gene signature** | • Gene signatures are seen as the future to enable multiplex testing algorithms for patients  
• $T_{\text{eff}}$ gene signature is equivalent to PD-L1 IHC |
| **TMB** | • tTMB: Pan tumor development for Tecentriq monotherapy (MYPATH, MX39795)  
• bTMB: Non-invasive biomarker for Tecentriq in 1L NSCLC (B-F1RST, B-FAST) |
| **NGS testing** | • Support NTRK pan-tumor, ROS1 in NSCLC, PI3K, PTEN alterations in breast cancer |

AC=all comers; Dx=diagnostic; TMB=tumor mutational burden; IHC=immunohistochemistry; NGS=next generation sequencing
Highlights late stage portfolio outside cancer immunotherapy

Sandra Horning, M.D.
Executive VP
Chief Medical Officer and Head Global Product Development
ASCO Highlights

Hematology

Breast

Lung
Late stage hematology
Improving standard of care and extending into new indications

Incidence rates (330,000 pts\(^1\))

- Ph III 1L (CLL14) + Venclexta
- Ph III R/R (MURANO)
- Ph II R/R (GO29365) + Polatuzumab vedotin
- Ph III 1L (POLARIX)
- Ph III R/R (MIRROS)
- Idasanutlin

1 Datamonitor; incidence rates includes the 7 major markets (US, Japan, France, Germany, Italy, Spain, UK); CLL=chronic lymphoid leukemia; DLBCL (aNHL)=diffuse large B-cell lymphoma; iNHL=indolent non-hodgkin’s lymphoma; AML=acute myeloid leukemia; MM=multiple myeloma; MDS=myelodysplastic syndrome; ALL=acute lymphoblastic leukemia; Venclexta in collaboration with AbbVie; Gazyva in collaboration with Biogen; Polatuzumab vedotin in collaboration with Seattle Genetics
**Venclexta + Rituxan in R/R CLL**

**MURANO results define new standard of care**

**Phase III results (MURANO) presented at ASH:**

- Primary PFS endpoint met (HR of 0.17) with benefit across all sub-groups, including high-risk patients
- OS HR of 0.48 with a descriptive p-value of 0.0186; Landmark 2Y OS at 91.9% for V+R vs 86.6% for B+R

Seymour et al., *NEJM* (2018); Hillmen P. *et al.*, ASCO 2018; Seymour J. *et al.*, ASH 2017; MRD= minimal residual disease; EP=end point; PB= peripheral blood; BM= bone marrow; ASO-PCR= allele-specific PCR; EOCT= end of combination treatment; PFS= progression free survival; HR= hazard ratio; OS= overall survival; V= Venclexta in collaboration with AbbVie; R= Rituxan; B= bendamustine
Venclexta + Rituxan in R/R CLL

PB MRD negativity maintained over time regardless of risk features

Phase III update (MURANO):

- PB MRD negativity kinetics for V+R are durable reflecting deep responses and correlate well with clinical outcome
- High PB MRD negativity for V+R achieved regardless of risk features (del17p, TP53mut, IGVH) contrary to B+R
- MURANO data filed in the US and EU; PDUFA date set for June 28
- Ph III (CLL14) results for Gazyva + Venclexta in 1L CLL expected in early 2019

Hillmen P. et al., ASCO 2018; PB MRD=peripheral blood minimal residual disease; PB MRD assessed by ASO-PCR and/or 8-color flow cytometry; PB MRD status was reported as follows: MRD+ if either ASO-PCR or flow-cytometry positive or if missing data or assay failure; V=Venclexta in collaboration with AbbVie; R=Rituxan; B=bendamustine
Venclexta + azacitidine/decitabine in 1L AML for older patients
Deep and durable responses regardless of risk status and age

<table>
<thead>
<tr>
<th>Cohort</th>
<th>N</th>
<th>ORR N (%)</th>
<th>CR/CRI N (%)</th>
<th>uMRD after CR/CRI n/N (%)</th>
<th>Median (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td>145</td>
<td>99 (68)</td>
<td>97 (67)</td>
<td>27/97 (29)</td>
<td>11.3 (8.9, NR)</td>
</tr>
<tr>
<td>V+aza/dec 400mg</td>
<td>60</td>
<td>44 (73)</td>
<td>44 (73)</td>
<td>17/44 (39)</td>
<td>12.5 (7.8, NR)</td>
</tr>
<tr>
<td>V+azacitidine</td>
<td>29</td>
<td>22 (76)</td>
<td>22 (76)</td>
<td>10/22 (45)</td>
<td>NR (5.6, NR)</td>
</tr>
<tr>
<td>V+decitabine</td>
<td>31</td>
<td>22 (71)</td>
<td>22 (71)</td>
<td>7/22 (32)</td>
<td>12.5 (5.1, NR)</td>
</tr>
<tr>
<td>V+aza/dec 800mg</td>
<td>74</td>
<td>50 (68)</td>
<td>48 (65)</td>
<td>10/48 (21)</td>
<td>11.0 (6.5, 12.9)</td>
</tr>
<tr>
<td>V+azacitidine</td>
<td>37</td>
<td>22 (59)</td>
<td>21 (57)</td>
<td>7/21 (33)</td>
<td>11.7 (4.6, 12.9)</td>
</tr>
<tr>
<td>V+decitabine</td>
<td>37</td>
<td>28 (76)</td>
<td>27 (73)</td>
<td>3/27 (11)</td>
<td>9.2 (5.9, NR)</td>
</tr>
<tr>
<td>Historical azacitidine</td>
<td>215</td>
<td>60 (28)</td>
<td></td>
<td></td>
<td>10.4</td>
</tr>
<tr>
<td>Historical decitabine</td>
<td>242</td>
<td>63 (26)</td>
<td></td>
<td></td>
<td>NR</td>
</tr>
</tbody>
</table>

**Phase Ib update (NCT02203773)**:

- Strong responses across risk subgroups and age >75 years compare favorably to historic results
- mOS not reached for the 400mg dose comparing favorably to historic results of 10.4m for aza and of 7.7m for dec
- 400mg V+aza/dec dose established due to best benefit-risk profile; Ph III (Viale-A) of V+aza in 1L AML on-going
- Accelerated filing of Ph Ib data expected by mid 2018

DiNardo C. D. et al., ASCO 2018; Kantarjian J Clin Onc 2012; Dombret Blood 2015; aza=azacitidine; dec=decitabine; ORR=overall response rate; CR=complete remission; CRi=complete remission with incomplete marrow recovery; uMRD=undetectable minimal residual disease (less than 10^-3 % leukemic cells as detected by multicolor flow cytometry in bone marrow aspirates at any measurement after achieving CR/CRi); mDOR=median duration of response; mOS=median overall survival; NR=not reached; V=Venclexta (in collaboration with AbbVie)
Polatuzumab vedotin + BR in R/R DLBCL

PFS/OS benefit regardless of prior treatment and disease status

<table>
<thead>
<tr>
<th></th>
<th>Pola + BR (N=40)</th>
<th>BR (N=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET-CR at EOT (%)</td>
<td>40</td>
<td>15</td>
</tr>
<tr>
<td>mPFS (months)</td>
<td>6.7 (4.9, 11.1)</td>
<td>2.0 (1.5, 3.7)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.31 (0.18, 0.55); p&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>2 L</td>
<td>11.1 (10.4, NE)</td>
<td>3.7 (1.5, 5.1)</td>
</tr>
<tr>
<td>3 L+</td>
<td>6.0 (4.0, 7.6)</td>
<td>2.0 (1.5, 2.8)</td>
</tr>
<tr>
<td>Relapsed</td>
<td>11.1 (10.4, NE)</td>
<td>5.1 (2.5, 10.0)</td>
</tr>
<tr>
<td>Refractory</td>
<td>6.0 (3.5, 7.4)</td>
<td>1.9 (1.1, 2.8)</td>
</tr>
<tr>
<td>mOS (months)</td>
<td>11.8 (9.5, NE)</td>
<td>4.7 (3.7, 8.3)</td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>0.35 (0.19, 0.67); p=0.0008</td>
<td></td>
</tr>
<tr>
<td>2 L</td>
<td>NR (10.5, NE)</td>
<td>5.9 (3.9, 8.4)</td>
</tr>
<tr>
<td>3 L+</td>
<td>11.5 (8.9, NE)</td>
<td>3.8 (3.2, 8.9)</td>
</tr>
<tr>
<td>Relapsed</td>
<td>NR (6.0, NE)</td>
<td>NR (NE, NE)</td>
</tr>
<tr>
<td>Refractory</td>
<td>11.5 (7.2, 12.4)</td>
<td>3.8 (3.2, 5.3)</td>
</tr>
</tbody>
</table>

Phase II update (GO29365):

- CR, PFS, OS were positive with a PFS HR of 0.31 (p<0.0001) and an OS HR of 0.35 (p=0.0008)
- OR, CR, PFS and OS were positive regardless of prior line of therapy (2L/3L+) or disease status (relapsed/refractory)
- Polatuzumab vedotin can be safely administered in combination with BR
- Accelerated filing of Ph II data expected in H2 2018

Sehn L. H. et al., ASCO 2018; PET-CR=posiotron emission tomography complete responses; EOT=end of treatment; mPFS=median progression free survival; mOS=median overall survival; HR=hazard ratio; OR=overall response; CR=complete response; Pola=polatuzumab vedotin (in collaboration with Seattle Genetics); BR=bendamustine + Rituxan
ASCO Highlights

Hematology

Breast

Lung
Ipatasertib + paclitaxel in 1L advanced TNBC

**PFS benefit and OS update**

**Ph II update (LOTUS):**

- PFS HR in all comers was 0.6 vs 0.44 for patients with PIK3CA/AKT1/PTEN-altered tumors as determined by FMI’s FoundationOne NGS assay
- Trend towards improved OS with a stratified OS HR in all comers of 0.62; Final OS results expected in 2019
- IPATunity130 (NCT03337724), a randomized phase III trial, is evaluating ipatasertib + paclitaxel as 1L treatment for PIK3CA/AKT1/PTEN-altered advanced TNBC (cohort 1) and in HR+/HER2- mBC (cohort 2)

Dent R. et al., ASCO 2018; PFS=progression free survival; OS=overall survival; ITT=intent to treat; HR=hazard ratio; FMI=Foundation Medicine; NGS=next generation sequencing; HR=hormone receptor; mBC=metastatic breast cancer
ASCO Highlights

Hematology

Breast

Lung
Alecensa in 1L ALK+ NSCLC

Alecensa currently more than triples PFS and DOR vs crizotinib

PFS* (ITT)

DOR* (responders)

Camidge D. R. et al, ASCO 2018; *Investigator assessment; PFS=progression free survival; ITT=intent to treat; DOR=duration of response; HR=hazard ratio; CNS=central nervous system; ORR=overall response rate; Alecensa (alectinib) in collaboration with Chugai

Ph III update (ALEX):

• Median PFS for Alecensa was 34.8m vs 10.9m for crizotinib with a stratified HR 0.43 and in patients with baseline CNS metastases median PFS was 27.7m vs 7.4m (HR 0.35). Median DOR for Alecensa was 33.1m vs 11.1m for crizotinib. OS data are still immature.
• Alecensa established as standard of care in 1L ALK+ NSCLC due to significantly improved efficacy and better safety
• Alecensa’s efficacy likely reflects more potent inhibition (also in the CNS), as well as suppression of common on-target resistance mechanisms

Camidge D. R. et al, ASCO 2018; *Investigator assessment; PFS=progression free survival; ITT=intent to treat; DOR=duration of response; HR=hazard ratio; CNS=central nervous system; ORR=overall response rate; Alecensa (alectinib) in collaboration with Chugai
Phase III oncology pipeline keeps expanding
31 trials and unique combinations across multiple diseases

* Venclexta in collaboration with AbbVie; Gazyva in collaboration with Biogen; Polatuzumab vedotin in collaboration with Seattle Genetics

**Lung: NSCLC, SCLC, ALK+NSCLC**
- 1L non-sq: Tecentriq + carbo/pac +/-Avastin IMpower130
- 1L non-sq: Tecentriq + carbo + nab-pac IMpower130
- 1L sq: Tecentriq + carbo + pac/nab-pac IMpower131
- 1L non-sq: Tecentriq + cis/carbo + pem IMpower132
- 1L Dx+: Tecentriq IMpower110
- Adj: Tecentriq IMpower010
- 1L SCLC: Tecentriq + carbo + etoposide IMpower133

**Melanoma**
- 1L BRAFwt: Tecentriq + Cotellic IMspire170
- 1L BRAFmut: Tecentriq + Cotellic + Zelboraf IMspire150 TRILOGY

**Renal**
- 1L: Tecentriq + Avastin IMmotion151
- Adj: Tecentriq IMmotion010

**Bladder**
- 1L: Tecentriq +/-gem/plat IMVigor130
- Adj: MIBC Tocentriq IMVigor010

**Prostate**
- 1L: ipatasertib + abiraterone IPATential180
- 2/3L: CRPC: Tocentriq + enzalutamide IMbassador250

**Head and neck**
- Adj SGCHN: Tocentriq +/-chemo IMvokata010

**Breast: TNBC; HER2+; ER+/HER2-**
- 1L TNBC: Tocentriq + nab-pac IMpassion130
- 1L TNBC: Tocentriq + pac IMpassion131
- Neo + ox TNBC: Tocentriq + nab-pac IMpassion031
- Adj TNBC: Tocentriq + paclitaxel IMpassion030
- 1L Dx+ TNBC: ipatasertib + paclitaxel IMpAmetry130 C1
- 1L Dx+ HR+ mBC: ipatasertib + paclitaxel IMpAmetry130 C2

**Hepatocellular carcinoma**
- 1L: Tocentriq IMbravo150

**Ovarian**
- 1L: Avastin/carbo/pac +/- Tocentriq IMGYN050

**Hematology: CLL, MM, AML, DLBCL**
- 1L CLL: Venclexta + Gazyva CLL14
- R/R CLL: Venclexta + Ruxuxin MURANO
- R/R MM: Venclexta + bortezomib/dexa BELLINI
- R/R AML: idasanutlin + cytarabine MIRROS
- 1L AML: Venclexta + azacitidine Vnda-A
- 1L AML: Venclexta + LDAC Vnda-C
- 1L DLBCL: polatuzumab vedotin + Ruxuxin-CHP POLARIX

= positive read-out
Oncology Strategy Update (Digital Health and PHC)

Daniel O’Day
CEO Roche Pharmaceuticals
Our innovation strategy remains unchanged
Accelerating data & advanced analytics efforts as central pillar of our strategy

Diverse, multidisciplinary talent base to drive innovation & execution
Rejuvenating the portfolio
Through continuously improving standard of care

### Replace existing businesses

<table>
<thead>
<tr>
<th>MabThera</th>
<th>Gazyva, Venclexta, polatuzumab vedotin, Sub Cut</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herceptin</td>
<td>Perjeta, Kadcyla, Sub Cut</td>
</tr>
<tr>
<td>Avastin</td>
<td>Tecentriq, entrectinib</td>
</tr>
<tr>
<td>Lucentis</td>
<td>VA2, port delivery</td>
</tr>
<tr>
<td>Tamiflu</td>
<td>baloxavir (Cap Endo)</td>
</tr>
</tbody>
</table>

### Entering new franchises

- **MS:** Ocrevus
- **Hemophilia:** Hemlibra
- **CNS:** SMA, Autism, Huntington’s

### ASCO / WFH 2018 highlights

- **Hemlibra:** HAVEN 3 / 4 with superior profile
  - IMpower150: OS benefit
  - IMpower 130: OS benefit
  - IMpower 131: PFS benefit
  - +Avastin in HCC: Meaningful responses
- **Venclexta:** MURANO in R/R CLL: New SoC showing high and durable MRD negativity
  - 1L AML (1b): Deep & durable responses
- **Polatuzumab:** R/R DLBCL: Strong efficacy confirmed
- **Ipatasertib:** LOTUS (Ph II) in TNBC: PFS benefit
- **Alecensa:** ALEX 1L ALK+: >34 months PFS benefit

VA2=anti-VEGF/anti-angiopoietin-2 bispecific antibody; MS=multiple sclerosis; SMA=spinal muscular atrophy; HCC=hepatocellular carcinoma; R/R CLL=relapsed/refractory (R/R) chronic lymphocytic leukemia; AML=acute lymphocytic leukemia; DLBCL=diffuse large B-cell lymphoma; TNBC=triple negative breast cancer; ALK=anaplastic lymphoma kinase
# Driving personalized healthcare forward

**Personalize treatment through understanding of a patient’s tumor**

<table>
<thead>
<tr>
<th>Blockbuster medicines</th>
<th>Targeted therapies</th>
<th>Personalized treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large: unspecified</td>
<td>Medium: sub-group</td>
<td>Small: individual patient</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Target population</th>
<th>Diagnostics</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No specific biomarkers</td>
<td>One medicine fits all</td>
</tr>
<tr>
<td></td>
<td>Single disease marker</td>
<td>Targeted agents</td>
</tr>
<tr>
<td></td>
<td>Comprehensive NGS &amp; response monitoring</td>
<td>Personalized combos of targeted &amp; CIT agents</td>
</tr>
</tbody>
</table>

NGS=Next generation sequencing; CIT=Cancer Immunotherapy

**Increasing need for advanced data analytics capabilities**
Data insights leveraged along the value chain
Foundation of future competitive differentiation

- Smarter, more efficient R&D
  - Biological insights & target identification
- Improved access & personalized patient care
  - Comprehensive Dx & personalized treatment options
- Improved regulatory & safety processes
  - Efficient trial design & recruitment
  - Clinical decision support
  - Value proof and reimbursement

Dx = Diagnostics
… creating direct & indirect value to our business

More effective R&D and more differentiated products

**Development**
- Lower costs
- Faster speed to market

**Commercial**
- Higher return

---

**Time (Years)**

**RETURN**

**INVESTMENT**

**‘PHC’ CURVE**

**‘CURRENT’ CURVE**

**Additional value**

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PHC=Personalized Healthcare
Acquisition of Flatiron

Leading player driving personalized patient care in oncology

**Strong network in Oncology**
- Leading EMR system and analytics solutions used by ~15% of US oncologists and covering ~15% of active patients

**Leading real world data base**
- Research-quality EMR data base covers 10m patients, over 2m of them active
- 90% of large Pharma companies are working with Flatiron data

While Flatiron will remain independent, acquisition will help to expand our existing partnership and provide required resources to accelerate key strategic projects in the field of personalized healthcare.

EMR = Electronic Medical Records
Generating new biologic insights and pan-tumor strategies

**PIK3CA/AKT1/PTEN-altered tumors in the LOTUS trial**

- Retrospectively identified PIK3CA/AKT1/PTEN-altered sub-population with increased benefit
  
  ![Graph showing survival rates and hazard ratios](image)
  
  - Unstratified HR: 0.44 (95% CI 0.20-0.99)
  - Median progression-free survival (mPFS): 4.9 months for ipatasertib + paclitaxel, 9.0 months for placebo + paclitaxel

- Utilizing FMI database to expand ipatasertib clinical trial program across different tumors
  
  - TNBC
  - HER2-/HR+
  - Others

- FMI key in identifying relevant patient sub-populations

---

FMI=Foundation Medicine; TNBC=Triple Negative Breast Cancer
Creating external control arm with RWD
Virtual control arm for Tecentriq in 2L NSCLC (OAK)

Retrospectively replicating docetaxel control arm in the Tecentriq OAK trial

Leveraging FH EMR data comprehensiveness & quality for more effective clinical development

RWD=Real World Data; NSCLC=Non Small Cell Lung Cancer; FH=Flatiron Healthcare; EMR=Electronic Medical Records
Leveraging RWD for regulatory approvals & HTA negotiations
Accelerating access and providing proof of value

Virtual control arm to supplement Alecensa in 2L ALK+ lung single-arm trials

NICE appraisal for Tecentriq in 2L NSCLC (OAK)

Leveraging FH EMR data in regulatory submissions and reimbursement discussions

RWD=Real World Data; HTA=Health Technology Assessment; NICE=National Institute for Health and Care Excellence; NSCLC=Non Small Cell Lung Cancer; FH=Flatiron Healthcare; ERG=Evidence Review Group; EMR=Electronic Medical Records
How to build true Meaningful Data at Scale?
nteenting complementary patient data will drive competitive advantage

<table>
<thead>
<tr>
<th>Deep genomic data</th>
<th>Broad, longitudinal patient data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human genomic profile</td>
<td>Medical records</td>
</tr>
<tr>
<td>Tumor genomic profile</td>
<td>Health &amp; wellbeing</td>
</tr>
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From a world with specific, disconnected databases…

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…to a world with truly integrated and meaningful data on each patient

Integrating deep and broad patient data has significant value potential to Roche and stakeholders
Our vision of personalized healthcare
*Leveraging large data and advanced analytics*

**Access meaningful data at scale**
- Clinical trial data
- Real world data

**Create insights through advanced analytics**

**Realize value from insights**
- Smarter, more efficient R&D
- Improved access & personalized care
Doing now what patients need next