53rd ASCO Annual Meeting, Chicago

Roche Analyst Event
Monday, 5 June 2017
This presentation contains certain forward-looking statements. These forward-looking statements may be identified by words such as ‘believes’, ‘expects’, ‘anticipates’, ‘projects’, ‘intends’, ‘should’, ‘seeks’, ‘estimates’, ‘future’ or similar expressions or by discussion of, among other things, strategy, goals, plans or intentions. Various factors may cause actual results to differ materially in the future from those reflected in forward-looking statements contained in this presentation, among others:

1. pricing and product initiatives of competitors;
2. legislative and regulatory developments and economic conditions;
3. delay or inability in obtaining regulatory approvals or bringing products to market;
4. fluctuations in currency exchange rates and general financial market conditions;
5. uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products;
6. increased government pricing pressures;
7. interruptions in production;
8. loss of or inability to obtain adequate protection for intellectual property rights;
9. litigation;
10. loss of key executives or other employees; and
11. adverse publicity and news coverage.

Any statements regarding earnings per share growth is not a profit forecast and should not be interpreted to mean that Roche’s earnings or earnings per share for this year or any subsequent period will necessarily match or exceed the historical published earnings or earnings per share of Roche.

For marketed products discussed in this presentation, please see full prescribing information on our website www.roche.com

All mentioned trademarks are legally protected.
Introduction

Karl Mahler
Head of Investor Relations
Agenda

Welcome
Karl Mahler, Head of Investor Relations

The APHINITY study: Adjuvant Pertuzumab and Herceptin in Initial Therapy in patients with HER2-positive early breast cancer
Jose Baselga, M.D., Ph.D., Physician-in-Chief and Chief Medical Officer, Memorial Hospital, MSKCC

Highlights late stage oncology pipeline
Sandra Horning, M.D., Chief Medical Officer and Head Global Product Development

Highlights early development
Ira Mellman, gRED: Ph.D., Vice President, Cancer Immunology, Genentech
William Pao, pRED: M.D., Ph.D., Global Head Oncology Discovery and Translational Area, Roche

Bringing innovation to patients
Daniel O’Day, CEO Roche Pharmaceuticals

Q&A
Roche growth supported by successful ongoing activities across entire portfolio

<table>
<thead>
<tr>
<th>Franchises</th>
<th>Enabling technologies</th>
</tr>
</thead>
</table>
| **Avastin** - CEA-TCB, combos with Tecentriq, MEKi etc. | **Cancer Immunotherapy**  
- Monotherapy (Tecentriq as backbone)  
- New antibody formats (TCBs)  
- Doublets/triplets  
- Combos with established agents |
| **HER2** - APHINITY: Perjeta in eBC, Kadcyla, Perjeta in mBC, subcutaneous | **Novel mAbs mono / combination** |
| **CD20** - CD20-TCB, Gazyva, Venclexta, ADCs, subcutaneous | **Novel targeted small molecules** |
| **Tecentriq** - 2/3L lung; 1/2L bladder | |
| **Ocrevus** - RMS, PPMS | |
| **Alecensa** - ALEX 1L, 2L Alk+ lung | |
| **Emicizumab** - HAVEN1 and 2 at ISTH | |
| **Tecentriq** - IMpower150 | |
| **Lampalizumab** - SPECTRI, CHROMA | |

Presented at ASCO 2017
Highlights late stage oncology pipeline

Sandra Horning, M.D.

Executive VP
Chief Medical Officer and Head Global Product Development
Portfolio progress

ASCO Highlights:

- Lung: Alecensa (ALEX); Tecentriq + chemo
- Renal: Tecentriq + Avastin (IMmotion150)
- Breast: Ipatasertib + chemo (LOTUS)

Oncology conclusions
Roche late-stage oncology pipeline

**Lung: NSCLC, SCLC, ALK+NSCLC**
- 2/3L: Tecentriq
- 1L non-sq: Tecentriq+carbo/pac+/−Avastin IMpower150
- 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
- 1L ALK+: Alecensa IMpower134
- OAK = approved

**Breast: TNBC; HER2+; ER+/HER2-**
- 1L TNBC: Tecentriq+nab-pac IMpassion130
- 1L TNBC: Tecentriq+pac IMpassion131
- Neoadj TNBC: Tecentriq+nab-pac IMpassion031
- Adj HER2+: Perjetc+Herceptin APHINITY
- ER+/HER2-: taselisib+fulvestrant SANDPIPER
- tba = ipatasertib

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

**Colorectal**
- 3L: Tecentriq+Cotellic IMblaze370

**Renal**
- 1L: Tecentriq+Avastin IMMmotion151
- Adj: Tecentriq IMMmotion010

**Ovarian**
- Front-line: Avastin/carbo/pac+/−Tecentriq IMaGYN050

**Prostate**
- 1L CRPC: ipatasertib+abiraterone IPATENTIAL150
- 2/3L CRPC: Tecentriq+enzalutamide IMbassador250

**Bladder**
- 1L/2L+: Tecentriq IMvigor210
- 1L: Tecentriq IMvigor210
- 2L+: Tecentriq IMvigor211
- 1L: Tecentriq+/−gem/plat IMvigor130
- Adj MIBC: Tecentriq IMvigor010

**Hematology: CLL, MM, AML**
- 1L CLL: Venclexta*+Gazyva CLL14
- R/R CLL: Venclexta*+Rituxan MURANO
- R/R MM: Venclexta*+bortezomib/dexa BELLINI
- R/R AML: idasanutin+cytarabine MIRROS
- 1L AML: Venclexta*+azacitidine NCT02993523
- tba

---
tba=to be announced; carbo=carboplatin; pac=paclitaxel; nab-pac=nab-paclitaxel (Abraxane); cis=cisplatin; pem=pemetrexed; gem=gemcitabine; plat=platinum; dextra=dexamethasone; *Venclexta in collaboration with AbbVie
12 cancer immunotherapy NMEs in the clinic

Multiple approaches across three tumor phenotypes

PCV* = personalised cancer vaccine in collaboration with BioNTech; 1 = in early development at Chugai; NME = new molecular entity; IND = new investigational drug application; TCB = T-cell bispecific; tba = to be announced.
Portfolio progress

ASCO Highlights:

- Lung: Alecensa (ALEX); Tecentriq + chemo
- Renal: Tecentriq + Avastin (IMmotion150)
- Breast: Ipatasertib + chemo (LOTUS)

Oncology conclusions
Late-stage oncology pipeline

**Robust lung cancer program**

### Lung: NSCLC, SCLC, ALK+NSCLC

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Drug(s)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/3 L</td>
<td>Tecentriq</td>
<td>OAK</td>
</tr>
<tr>
<td>1 L non-sq</td>
<td>Tecentriq+carbo/pac+/-Avastin</td>
<td>IMpower150</td>
</tr>
<tr>
<td>1 L non-sq</td>
<td>Tecentriq+carbo+nab-pac</td>
<td>IMpower130</td>
</tr>
<tr>
<td>1 L sq</td>
<td>Tecentriq+carbo/pac/nab-pac</td>
<td>IMpower131</td>
</tr>
<tr>
<td>1 L non-sq</td>
<td>Tecentriq+cis/carbo+perm</td>
<td>IMpower132</td>
</tr>
<tr>
<td>1 L Dx+</td>
<td>Tecentriq</td>
<td>IMpower110</td>
</tr>
<tr>
<td>Adj</td>
<td>Tecentriq</td>
<td>IMpower010</td>
</tr>
<tr>
<td>1 L SCLC</td>
<td>Tecentriq+carbo/etoposide</td>
<td>IMpower133</td>
</tr>
<tr>
<td>1 L ALK+</td>
<td>Alecensa</td>
<td>ALEX; J-ALEX</td>
</tr>
</tbody>
</table>

### Breast: TNBC; HER2+; ER+/HER2-

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Drug(s)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 L TNBC</td>
<td>Tecentriq+nab-pac</td>
<td>IMpassion130</td>
</tr>
<tr>
<td>1 L TNBC</td>
<td>Tecentriq+pac</td>
<td>IMpassion131</td>
</tr>
<tr>
<td>Neoadj TNBC</td>
<td>Tecentriq+nab-pac</td>
<td>IMpassion031</td>
</tr>
<tr>
<td>Adj HER2+</td>
<td>Perjeta+Herceptin</td>
<td>APHINITY</td>
</tr>
<tr>
<td>ER+/HER2-</td>
<td>taselaib+fulvestrant</td>
<td>SANDPIPER</td>
</tr>
</tbody>
</table>

### Colorectal

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Drug(s)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 L</td>
<td>Tecentriq+Cotellic</td>
<td>IMblaze370</td>
</tr>
</tbody>
</table>

### Ovarian

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Drug(s)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Front-line</td>
<td>Avastin/carbo/pac+/-Tecentriq</td>
<td>IMaGYN050</td>
</tr>
</tbody>
</table>

### Prostate

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Drug(s)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 L CRPC</td>
<td>ipatasertib+abiraterone</td>
<td>IPATENTIAL150</td>
</tr>
<tr>
<td>2/3 L CRPC</td>
<td>Tecentriq+enzalutamide</td>
<td>IMbassador250</td>
</tr>
</tbody>
</table>

### Hematology: CLL, MM, AML

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Drug(s)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 L CLL</td>
<td>Venclexta+/Gazyva</td>
<td>CLL14</td>
</tr>
<tr>
<td>R/R CLL</td>
<td>Venclexta+/Rituxan</td>
<td>MURANO</td>
</tr>
<tr>
<td>R/R MM</td>
<td>Venclexta+/bortezomib/dexa</td>
<td>BELLINI</td>
</tr>
<tr>
<td>R/R AML</td>
<td>idasanutin+cytarabine</td>
<td>MIRROS</td>
</tr>
<tr>
<td>1 L AML</td>
<td>Venclexta+/azacitidine</td>
<td>NCT02983523</td>
</tr>
</tbody>
</table>

= approved
Alecensa in 1L ALK+ NSCLC: ALEX study

Results confirm Alecensa as new standard of care

**Ph III ALEX results**

- Compared to crizotinib, Alecensa significantly prolonged PFS, delayed time to CNS progression, improved intracranial ORR and DOR and had a more favorable safety profile
- The clinical benefit of Alecensa over crizotinib likely reflects more potent target inhibition, particularly in the CNS, as well as suppression of common on-target resistance mechanisms
- J-ALEX update: Alecensa more than doubled PFS compared to crizotinib with favorable safety

Shaw A. *et al*, ASCO 2017; *Investigator assessment; Alecensa (alectinib) in collaboration with Chugai; ITT=intent to treat; CNS=central nervous system; HR=hazard ratio; PFS=progression free survival; ORR=overall response rate; DOR=duration of response
**Tecentriq + chemo in 1L sq/non-sq NSCLC**

*Ph I data support chemo combo program*

### Response rates

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>9 (36)</td>
<td>17 (68)</td>
<td>12 (46)</td>
</tr>
<tr>
<td>CR</td>
<td>0</td>
<td>1 (4)</td>
<td>4 (15)</td>
</tr>
<tr>
<td>PR</td>
<td>9 (36)</td>
<td>16 (64)</td>
<td>8 (31)</td>
</tr>
<tr>
<td>SD</td>
<td>12 (48)</td>
<td>4 (16)</td>
<td>9 (35)</td>
</tr>
<tr>
<td>PD</td>
<td>3 (12)</td>
<td>3 (12)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Unevaluable</td>
<td>1 (4)</td>
<td>1 (4)</td>
<td>2 (8)</td>
</tr>
</tbody>
</table>

### Overall survival (OS)

![Overall survival graph]

**Ph I results**

- Encouraging mOS, ORRs including CRs
- IMpower150 (Ph III testing Tecentriq + carboplatin/paclitaxel and Tecentriq + Avastin + carboplatin/paclitaxel) expected to read out in H2 2017
- 4 additional Ph III 1L (NSCLC and SCLC) studies expected to read out in 2018

Liu S. *et al.*, ASCO 2017; cb=carboplatin; pac=paclitaxel; cp=cisplatin, pem=pemetrexed; nab=nab-paclitaxel (Abraxane); ORR=overall response rate; CR=complete response; PR=partial response; SD=stable disease; PD=progressive disease
Roche CIT lung cancer program
Addressing all market segments

IMpower133¹
(Tecentriq+cb+etoposide)
(2018)

IMpower131
(Tecentriq+cb+pac/nab-pac)
(2018)

IMpower150
(Tecentriq+cb/pac+/-Avastin)
(2017)

IMpower130
(Tecentriq+cb+nab-pac)
(2018)

IMpower132
(Tecentriq+cp/cb+pem)
(2018)

= Roche first-to-market with chemo combo

Tecentriq + chemotherapy has the potential to be first-to-market chemo combo in SCLC and squamous NSCLC (45% of the total market)

Source: Datamonitor; incidence rates 7 major markets (US, Japan, France, Germany, Italy, Spain, UK); Note: Outcome studies are event driven, timelines may change; ¹IMpower133 in extensive stage SCLC; CIT=cancer immunotherapy; NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer
Portfolio progress

ASCO Highlights:

- Lung: Alecensa (ALEX); Tecentriq + chemo
- Renal: Tecentriq + Avastin (IMmotion150)
- Breast: Ipatasertib + chemo (LOTUS)

Oncology conclusions
Late-stage oncology pipeline

**First results from Tecentriq+Avastin in mRCC**

**Lung:**
- NSCLC, SCLC, ALK+NSCLC
  - 2/3L: Tecentriq
  - 1L non-sq: Tecentriq+carbo/pac+/-Avastin
  - 1L non-sq: Tecentriq+carbo+nab-pac
  - 1L sq: Tecentriq+carbo/pac/nab-pac
  - 1L non-sq: Tecentriq+cli/carbo+pe
  - 1L Dx+: Tecentriq
  - Adj: Tecentriq
  - 1L SCLC: Tecentriq+carbo+etoposide
  - 1L ALK+: Alecensa

**Breast:**
- TNBC; HER2+; ER+/HER2-
  - 1L TNBC: Tecentriq+nab-pac
  - 1L TNBC: Tecentriq+pe
  - Neoadj TNBC: Tecentriq+nab-pac
  - Adj HER2+: Perjeta+Herceptin
  - ER+/HER2-: taselisib+fulvestrant

**Colorectal:**
- 3L: Tecentriq+Cotellic

**Melanoma:**
- Adj: Zelboraf
- 1L BRAFwt: Tecentriq+Cotellic
- 1L BRAFmut: Tecentriq+Cotellic+Zelboraf

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

**Bladder:**
- 1L/2L+: Tecentriq
- 1L: Tecentriq
- 2L+: Tecentriq
- 1L: Tecentriq+/-gem/plat
- Adj MIBC: Tecentriq

**Prostate:**
- 1L CRPC: ipatasertib+abiraterone
- 2/3L CRPC: Tecentriq+enzalutamide

**Hematology:**
- CLL, MM, AML
  - 1L CLL: Venclexta*+Gazyva
  - R/R CLL: Venclexta*+Rituxan
  - R/R MM: Venclexta*+bortezomib/dexa
  - R/R AML: idasanutin+cytarabine
  - 1L AML: Venclexta*+azacitidine

**Notes:**
- = approved
Ph II IMmotion150 results

- Median PFS for Tecentriq + Avastin was 11.7m in the ITT population and 14.7m in the PD-L1+ population, comparing favorably with sunitinib monotherapy or Tecentriq monotherapy.
- Higher ORR with combinations; median DOR not reached at a median follow-up of 20.7m.
- Results of the phase III study IMmotion151 (T + A versus sunitinib) expected early 2018.

Atkins M. et al., ASCO 2016; Clinical cut-off, Oct 17, 2016. Median follow-up: 20.7m; ITT=intent-to-treat; PFS=progression free survival; IC=immune cell; HR=hazard ratio; ORR=overall response rate; DOR=duration of response; T=Tecentriq; A=Avastin.
Tecentriq + Avastin in 1L advanced mRCC
Clinically meaningful activity after crossover

IMmotion150 crossover analysis
- Clinically meaningful 2L activity regardless of 1L therapy and 1L response; supports combination therapy
- ORR of 26% in all crossover patients (28% for 1L sunitinib and 24% for 1L Tecentriq)
- mPFS of 8.8m for all crossover patients matches or exceeds outcomes from 1L monotherapy

Atkins M. et al., ASCO 2016; Clinical cut-off date: Oct 17, 2016. Median duration of follow-up for all crossover: 12.7 months; ORR=overall response rate; PFS=progression free survival
Portfolio progress

ASCO Highlights:

- Lung: Alecensa (ALEX); Tecentriq + chemo
- Renal: Tecentriq + Avastin (IMmotion150)
- Breast: Ipatasertib + chemo (LOTUS)

Oncology conclusions
Late-stage oncology pipeline

**Ipatasertib: Highly selective activated AKT inhibitor**

<table>
<thead>
<tr>
<th>Lung: NSCLC, SCLC, ALK+NSCLC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/3L</td>
</tr>
<tr>
<td>1L non-sq</td>
</tr>
<tr>
<td>1L non-sq</td>
</tr>
<tr>
<td>1L sq</td>
</tr>
<tr>
<td>1L non-sq</td>
</tr>
<tr>
<td>1L Dx+</td>
</tr>
<tr>
<td>Adj</td>
</tr>
<tr>
<td>1L SCLC</td>
</tr>
<tr>
<td>1L ALK+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Breast: TNBC; HER2+; ER+/HER2-</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L TNBC</td>
</tr>
<tr>
<td>1L TNBC</td>
</tr>
<tr>
<td>Neoadj TNBC</td>
</tr>
<tr>
<td>Adj HER2+</td>
</tr>
<tr>
<td>ER+/HER2- taselisib+fulvestrant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Colorectal</th>
</tr>
</thead>
<tbody>
<tr>
<td>3L</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ovarian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Front-line</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L</td>
</tr>
<tr>
<td>Adj</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bladder</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L/2L+</td>
</tr>
<tr>
<td>1L</td>
</tr>
<tr>
<td>2L+</td>
</tr>
<tr>
<td>1L</td>
</tr>
<tr>
<td>Adj MIBC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Prostate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L CRPC</td>
</tr>
<tr>
<td>2/3L CRPC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hematology: CLL, MM, AML</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L CLL</td>
</tr>
<tr>
<td>R/R CLL</td>
</tr>
<tr>
<td>R/R MM</td>
</tr>
<tr>
<td>R/R AML</td>
</tr>
<tr>
<td>1L AML</td>
</tr>
</tbody>
</table>

= approved
Ipatasertib + chemo in 1L TNBC

Strong benefit in PIK3CA/AKT1/PTEN-altered tumors

**Ph II LOTUS results**
- PFS HR in the ITT population was 0.6 compared to 0.44 for patients with PIK3CA/AKT1/PTEN-altered tumors by FoundationOne NGS assay
- Phase III development of ipatasertib underway

Dent R. *et al.*, ASCO 2017; PFS=progression free survival; ITT=intent to treat; HR=hazard ratio; NGS=next generation sequencing
FoundationOne NGS Assay
Lead diagnostic for ipatasertib in TNBC

NGS assay designed to detect genetic alterations in >300 oncogenes

LOTUS population segmented based on PI3K/Akt pathway status

Ph II LOTUS results

- NGS assay allowed a broad survey of the mutational landscape in TNBC
- Greatest benefit for ipatasertib + chemotherapy in PIK3CA/AKT1/PTEN-altered tumors, identified with the FMI NGS assay
- Partnership with FMI enables rapid transition from research-based findings to diagnostic development

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>PFS HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unselected</td>
<td>124</td>
<td>0.60</td>
</tr>
<tr>
<td>ITT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventana IHC assay</td>
<td>48</td>
<td>0.68</td>
</tr>
<tr>
<td>PTEN-low</td>
<td>54</td>
<td>0.54</td>
</tr>
<tr>
<td>PTEN-high</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NGS FMI assay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PIK3CA/AKT1/PTEN-altered</td>
<td>42</td>
<td>0.44</td>
</tr>
<tr>
<td>P/A/P-non-altered</td>
<td>61</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Dent R. et al., ASCO 2017; NGS=next generation sequencing; PFS=progression free survival; HR=hazard ratio; FMI=Foundation Medicine
Portfolio progress

ASCO Highlights:

- **Lung:** Alecensa (ALEX); Tecentriq + chemo
- **Renal:** Tecentriq + Avastin (IMmotion150)
- **Breast:** Ipatasertib + chemo (LOTUS)

Oncology conclusions
MORPHEUS: Novel CIT platform
Efficient & confident combo development

Multi-indication
"One protocol per tumor"

Multi-basket
"All-comers" and "Biomarker defined subgroup refinement"

Randomized
"Signals always evaluated vs SOC to improve confidence"

Longitudinal
"Reverse-translational science with mandatory biopsies prior to 2L treatment"

Adaptable
"Add or remove combinations via planned amendments"

NSCLC
Pancreatic
Gastric
HR+ BC
TNBC
CRC
UBC

1L all-comers
2L all-comers
Biomarker

Combo 1
Combo 2
Combo 3
SOC control

Combo 2
Combo 3

Combo 4
Combo 5
Combo 6

Faster and more confident decisions
Potential for accelerated approval

CIT=cancer immunotherapy; SOC=standard of care
MORPHEUS: Novel CIT platform

First trials add depth to our CIT strategy

2017 launch in 5 indications
including 9 molecules and 17 first-in-disease combinations

CIT=cancer immunotherapy; NME=new molecular entity; TCB=T-cell bi-specific
Snapshots of internal assets and combinations

Launched portfolio

Venclexta in collaboration with AbbVie; Gazyva in collaboration with Biogen; Alecensa in collaboration with Chugai; Cotellic in collaboration with Exelixis; Zelboraf in collaboration with Plexxikon; polatuzumab in collaboration with Seattle Genetics; ipatasertib in collaboration with Array Biopharma; IDOi in collaboration with NewLink; daratumumab in collaboration with Janssen (J&J); NME=new molecular entity; PCV=personalized cancer vaccine; TCB=T-cell bi-specific

Status: June 2017

Taselenib

Ipatasertib

Herceptin (trastuzumab)

Kadcyla (ad-trastuzumab emtansine)

Perjeta (pertuzumab)

Rituxan (rituximab)

Tecentriq (atezolizumab)

Gazyva (obinutuzumab)

Alecensa (alec替尼)

Tarceva (erlotinib)

Venclexta (venetoclax)

Idasanutlin

Polatuzumab vedotin

aCSF1R

aCEA-IL2v FP

aFAP-IL2v FP

aCD40

aOX40

IDOi

aCEA-TCB

aCD20-TCB1

aCD20-TCB2

aTIGIT

PCV

glypican3-TCB

Combination approved

Combination in development

Roche NME late stage

Roche NME early stage

Non-Roche approved drugs

Chugai NME early stage
gRED: The next wave of cancer immunotherapy

Ira Mellman, Ph.D.
Vice President, Cancer Immunology, Genentech
gRED's CIT portfolio

Wave 1: Targets for patients with pre-existing immunity

Wave 2: Inducing immunity in patients who have none
Targeting treatment options to different patients and cancer types

**IMMUNE INFLAMED**
CD8+ T cells infiltrated, but non-functional
Accelerate or remove brakes on T-cell response
e.g. Tecentriq, Cotelic, navoximod (IDOi), aOX40, aTIGIT, aCEA/FAP
IL-2v, aCSF-1R, TCBs (CEA TCB, CD20 TCB)

**IMMUNE EXCLUDED**
CD8+ T cells accumulated but have not efficiently infiltrated
Bring T-cells in contact with cancer cells
e.g. aVEGF, TCBs (CEA TCB, CD20 TCB)

**IMMUNE DESERT**
CD8+ T cells absent from tumor and periphery
Increase number of antigen-specific T-cells or increase antigen presentation
e.g. aCD40, chemotherapy, radiotherapy, targeted therapies, TCBs (CEA TCB, CD20 TCB), PCV

TCB=T cell bispecific, PCV=personalized cancer vaccine
gRED’s next-generation pipeline targets
*Five novel CIT assets under evaluation*

<table>
<thead>
<tr>
<th><strong>aTIGIT</strong></th>
<th><strong>IDOi</strong></th>
<th><strong>CD20-TCB</strong></th>
<th><strong>aOX40</strong></th>
<th><strong>PCV</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-TIGIT MAb enhances effector T cell responses to tumors by blockade of the receptor-ligand pair TIGIT-PVR.</td>
<td>IDO-selective small molecule inhibitor.</td>
<td>Full-length bispecific antibody that targets CD20 on B cells and CD3 on T cells.</td>
<td>Agonist MAb that targets OX40 costimulatory receptor on antigen-experienced T cells.</td>
<td>PCVs use a patient’s unique neo-antigens to induce an anti-tumor immune response.</td>
</tr>
</tbody>
</table>

"Synthetic immunity"

*in collaboration with NewLink
TCB=T cell bispecific, PCV=personalized cancer vaccine
gRED's CIT portfolio

Wave 1: Targets for patients with pre-existing immunity

Wave 2: Inducing immunity in patients who have none
Navoximod (IDOi) + Tecentriq

First clinical data in solid tumors

Ph I results: Early evidence of clinical activity

- Heterogeneous patient population with mix of inflamed and non-inflamed tumors (any PD-L1+ 44%*)
  - 6 patients with a PR (melanoma, pancreatic, prostate, ovarian, HNSCC, cervical)
- Combination is well tolerated with low treatment discontinuations
- Expansion phase enrolling at navoximod 600mg and 1000mg BID with Tecentriq

Data cut-off date 14 Feb 2017; * Nine patients (15%) PD-L1 IHC data unavailable; † 3L ovarian cancer patient with 41% reduction in target lesion by Day 84 (C4). Patient was treated with 1000mg navoximod (GDC-0919) single agent for 1 cycle (21days) prior to starting combination treatment at 600mg.
MEKi is an unexpected combo partner for anti-PD-L1

Blocks naive T cell priming & inhibits T cell exhaustion

**MEK inhibitors potentiate anti-tumor T cells**

- **Naive T cell**
- **Short term memory T cell**
- **Effector T cell**
- **Target killing**

**MEKi causes class I MHC upregulation**

- **Exhausted T cell**

MEKi inhibition, via direct effects on T cells and the tumor microenvironment, may help to unlock the full anti-tumor potential of PD-L1 inhibition.

Ebert et al. *Immunity* 2016;
MHC=major histocompatibility complex
Tecentriq + Cotelllic in 1L metastatic melanoma

**mPFS of 15.7 months encouraging**

### Best objective response, RECIST v1.1

<table>
<thead>
<tr>
<th></th>
<th>Tecentriq + Cotelllic&lt;sup&gt;1&lt;/sup&gt; (N=20), n (%)</th>
<th>Tecentriq&lt;sup&gt;2&lt;/sup&gt; (N=37), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Line of therapy</strong></td>
<td>1L (50%)</td>
<td>1L (38%)</td>
</tr>
<tr>
<td></td>
<td>2L (10%)</td>
<td>2L (19%)</td>
</tr>
<tr>
<td></td>
<td>≥3L (40%)</td>
<td>≥3L (44%)</td>
</tr>
<tr>
<td>% BRAF wild type</td>
<td>10 (50%)</td>
<td>49%</td>
</tr>
<tr>
<td>% BRAF-mutant</td>
<td>10 (50%)</td>
<td>27%</td>
</tr>
<tr>
<td>CR/PR</td>
<td>9 (45%)</td>
<td>32%</td>
</tr>
<tr>
<td>SD</td>
<td>6 (30%)</td>
<td>27%</td>
</tr>
<tr>
<td>PD</td>
<td>5 (25%)</td>
<td>28%</td>
</tr>
<tr>
<td>mPFS (months)</td>
<td>15.7</td>
<td>5.5</td>
</tr>
</tbody>
</table>

### Ph I results

- Higher ORR and longer PFS may be achieved with Tecentriq + Cotelllic vs. Tecentriq monotherapy
- Doublet has a manageable safety profile
- Immune contexture may be altered by Cotelllic, enhancing Tecentriq’s activity

1 Miller W. et al, ASCO 2017 [abstract 3057]; 2 Hodi et al. Pigment Cell Melanoma Res 2014; Cotelllic in collaboration with Exelixis

CR=complete response; PR=partial response; SD=stable disease; PD=progressive disease; PFS=progression free survival
Tecentriq + Zelboraf + Cotelpic in 1L *BRAF*+ mM

*Early data show a 82% ORR*

<table>
<thead>
<tr>
<th>Best objective response, RECIST v1.1</th>
<th>T + Z + C (N=38), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>31 (82%)</td>
</tr>
<tr>
<td>CR</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>PR</td>
<td>24 (63%)</td>
</tr>
<tr>
<td>SD</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>PD</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Non-evaluable</td>
<td>2 (7%)</td>
</tr>
</tbody>
</table>

**Ph I results**

- Triplet has a manageable safety profile
- Estimated median duration of response 10.6m and mPFS 12.9m (data immature)
- Triplet expected to differentiate on durability
- Evidence of an association between OS and T effector signature, *CD8A* and *PD-L1*

**Reduction in tumor burden**

**Change in tumor burden over time**

---

Sullivan R. *et al*, ASCO 2017 [abstract 3063]; Cotelpic in collaboration with Exelxis; Zelboraf in collaboration with Plexxikon; mM=metastatic melanoma; ORR=overall response rate; CR=complete response; PR=partial response; SD=stable disease; PD=progressive disease
gRED's CIT portfolio

Wave 1: Targets for patients with pre-existing immunity

Wave 2: Inducing immunity in patients who have none
Targeting treatment options to different patients and cancer types

<table>
<thead>
<tr>
<th>Melanoma</th>
<th>Lung</th>
<th>Bladder</th>
<th>TNBC</th>
<th>Colorectal</th>
<th>Gastric</th>
<th>Ovarian</th>
</tr>
</thead>
</table>

**IMMUNE INFLAMED**
CD8+ T cells infiltrated, but non-functional

Accelerate or remove brakes on T-cell response

e.g. Tecentriq, Cotellic, navoximod (IDOi), aOX40, aTIGIT, aCEA/FAP
IL-2v, aCSF-1R, TCBs (CEA TCB, CD20 TCB)

**IMMUNE EXCLUDED**
CD8+ T cells accumulated but have not efficiently infiltrated

Bring T-cells in contact with cancer cells

e.g. aVEGF, TCBs (CEA TCB, CD20 TCB)

**IMMUNE DESERT**
CD8+ T cells absent from tumor and periphery

Increase number of antigen-specific T-cells or increase antigen presentation

e.g. aCD40, chemotherapy, radiotherapy, targeted therapies, TCBs (CEA TCB, CD20 TCB), PCV

TCB=T cell bispecific, PCV=personalized cancer vaccine
Predicting immunogenic tumor mutations
Only few mutations elicit T cell immunity

Mutated neo-antigens are the drivers of immune responses against cancer. Is there promise for an individualized cancer vaccine?

Indication response rates correlate with mutation frequency

Mutant peptide-MHCI complexes

Immunogenic
AQL[A/P]NDVVL

Less-immunogenic
SIIVFNL[L/V]

Kandoth et al., Nature 2013; Yadav et al., Nature 2014
Expanding gRED’s drug discovery platform

Personalized cancer vaccine to mobilize immunity

- **Fully individualized vaccine** (mRNA-based approach)
- **On demand—production** (highly iterated and reproducible with low failure rate)
- Suitable for potentially all tumor indications, also with low incidences
- No negative thymic selection of high-affinity TCRs against mutated epitopes
- Induction of immune responses with high tumor specificity

4 weeks
Initial monitoring data for melanoma patients

Majority of RNA-neoepitopes are immunogenic

Liposomal PCV-mRNA is delivered to dendritic cells; the optimal destination to prime T cells

PCV induces T cell immunity

<table>
<thead>
<tr>
<th>Neoeptopes</th>
<th>T cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>32% de novo</td>
<td>26%</td>
</tr>
<tr>
<td>68% pre-formed</td>
<td>57%</td>
</tr>
</tbody>
</table>

Lymph node lesions with signs of tumor necrosis

Pre-vaccination: Normal tissue, Tumor tissue, Necrosis
Post-vaccination: Normal tissue, Tumor tissue, Necrosis

Phase I combination study of PCV and Tecentriq to start in 2017

Presented by BioNTech, AACR 2017;

MRT imaging after 12 months vaccination (patient was rated as a partial remission); PCV=Personalized cancer vaccine
pRED: The next wave of cancer immunotherapy

William Pao, M.D., Ph.D.
Global Head Oncology Discovery and Translational Area, Roche pRED
pRED’s next-generation CIT pipeline molecules
Novel MoAs; multiple combination opportunities

<table>
<thead>
<tr>
<th>CEA-TCB</th>
<th>CD20-TCB</th>
<th>CEA-IL2v FP</th>
<th>FAP-IL2v FP</th>
<th>aCD40</th>
<th>aCSF-1R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engage and activate T cells to kill tumors cells using novel 2:1 TCB format</td>
<td></td>
<td>Modulate (amplify) immune response by delivery of tumor-targeted recombinant immunocytokine (IL-2)</td>
<td></td>
<td>Generate more tumor-killing antigen-specific T cells</td>
<td>Modulate immune response by eliminating immunosuppressive tumor-associated macrophages</td>
</tr>
</tbody>
</table>

CEA=Carcinoembryonic antigen; TCB=T cell bispecific; FP=Fusion Protein
Images created by Alexander Bujotzek
pRED’s next-generation CIT pipeline molecules
Novel MoAs; multiple combination opportunities

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA-TCB</td>
<td>Engage and activate T cells to kill tumors cells using novel 2:1 TCB format</td>
</tr>
<tr>
<td>CD20-TCB</td>
<td>Modulate (amplify) immune response by delivery of tumor-targeted recombinant immunocytokine (IL-2)</td>
</tr>
<tr>
<td>CEA-IL2v FP FAP-IL2v FP</td>
<td>Generate more tumor-killing antigen-specific T cells</td>
</tr>
<tr>
<td>aCD40</td>
<td>Modulate immune response by eliminating immunosuppressive tumor-associated macrophages</td>
</tr>
<tr>
<td>aCSF-1R</td>
<td></td>
</tr>
</tbody>
</table>

CEA=Carcinoembryonic antigen; TCB=T cell bispecific; FP=Fusion Protein

Images created by Alexander Bujotzek
CEA-TCB (CEA/CD3 TCB) is the first T-cell bispecific antibody with a novel 2-to-1 format, optimized for efficacy and safety

- Binds simultaneously with one arm to CD3 on T-cells and with two arms to CEA on tumor cells
- Flexible 2-to-1 format enables high avidity binding and selective killing of high CEA-expressing tumor cells
- Longer half-life compared to other TCB formats
- Silent Fc results in reduced risk of FcγR-related cytokine release/IRRs

2:1 format allows flexible range of motion in Fabs\(^a,1,2\)

Anti-PD-L1 enhances anti-tumor activity of CEA-TCB\(^3\)

- PD-L1 is upregulated upon IFNγ secretion, providing rationale for combining CEA-TCB with atezolizumab\(^2\)

---


IRR=immune-related reaction
CEA-TCB may overcome challenges in CIT
Potential across three major categories of solid tumors

INFLAMED

CD8+ T cells infiltrated, but non-functional

Accelerate or remove brakes on T-cell response

IMMUNE EXCLUDED

CD8+ T cells accumulated but have not efficiently infiltrated

Bring T-cells in contact with cancer cells

IMMUNE DESERT

CD8+ T cells absent from tumor and periphery

Increase number of antigen-specific T-cells or increase antigen presentation

CEA-TCB: First 2-to-1 T cell bispecific in the clinic
Two phase 1 studies ongoing

<table>
<thead>
<tr>
<th>Study 1: CEA-TCB monotherapy (IV qw)</th>
<th>Study 2: CEA-TCB (IV qw) + Tecentriq (1200 IV q3w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SAD</strong></td>
<td><strong>All</strong></td>
</tr>
<tr>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td><strong>MAD</strong></td>
<td>75</td>
</tr>
<tr>
<td><strong>MAD</strong></td>
<td>45</td>
</tr>
</tbody>
</table>

**Basis for safety data presented:**
- All tumor types
- **Study 1:** CEA-TCB monotherapy; 80 patients treated at all doses, including 59 patients treated ≥ 40 mg
- **Study 2:** CEA-TCB + Tecentriq; 45 patients treated at all doses, including 33 patients treated ≥ 40 mg

**Basis for efficacy data presented:**
- CRC only
- **Study 1:** CEA-TCB monotherapy; 31 patients (of 65, MAD only) treated at 60 - 600 mg with on-treatment tumor assessment
- **Study 2:** CEA-TCB + Tecentriq; 25 patients (of 35) treated at 5 to 160 mg with on-treatment tumor assessment

Tabernero et al. ASCO 2017, abstract 3002; oral presentation 5 June 2017


* Due to DLT at 40 mg in study 1 in a NSCLC patient, safety data cut-off is ≥ 40 mg.

* Radiological signs of tumor inflammation seen at ≥ 60 mg.

CRC=colorectal cancer; Eso=esophageal cancer; NSCLC=non-small cell lung cancer; PaC=pancreatic cancer; SAD=single ascending dose; MAD=Multiple ascending dose
Focus on mCRC, of which >90% express high CEA

Poor treatment options in heavily pre-treated patients

OS for CORRECT and RECOURSE trials in refractory mCRC

<table>
<thead>
<tr>
<th>Confirmed response</th>
<th>Regorafenib (N=505)</th>
<th>TAS-102 (N=221)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>1.0%</td>
<td>1.6%</td>
</tr>
<tr>
<td>DCR</td>
<td>41%</td>
<td>44%</td>
</tr>
<tr>
<td>mPFS</td>
<td>1.9 mo</td>
<td>2.0 mo</td>
</tr>
<tr>
<td>mOS</td>
<td>6.4 mo</td>
<td>7.1 mo</td>
</tr>
</tbody>
</table>

- Limited efficacy of regorafenib and TAS-102 (current SOC) in mCRC patients after failure of all standard lines of therapy
- Adverse event profiles of regorafenib and TAS-102 require monitoring and dose modifications

~ 95% of MSS patients do not appear to benefit from checkpoint inhibitors

On treatment biopsies suggest that CEA-TCB leads to T-cell engagement, activation, and proliferation.

**CEA-TCB increases the number of PD-1+ T cells in tumors**

<table>
<thead>
<tr>
<th>Patient</th>
<th>RECIST v1.1 response</th>
<th>BSL</th>
<th>OT</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>-68%</td>
<td>5%</td>
<td>21%</td>
</tr>
<tr>
<td>b</td>
<td>7%</td>
<td>14%</td>
<td>12%</td>
</tr>
</tbody>
</table>

%PD-1+/CD8+ gated on live CD45+/CD3+ cells

**CEA-TCB induces increases of proliferating T cells**

<table>
<thead>
<tr>
<th>CEA-TCB dose</th>
<th>Log2 (CD3+/Ki67+ T-cells/mm² tumor area)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-90mg</td>
<td></td>
</tr>
<tr>
<td>≥135mg</td>
<td></td>
</tr>
</tbody>
</table>

Biopsies were assessed by IHC and analyzed using an in-house automated digital platform (IRIS); (p=0.035, 3.6 fold increase)

Similar results seen with study 2: CEA-TCB + Tecentriq

Melero et al. ASCO 2017, abstract 2549; poster presentation on 5 June, 2017, 8:00-11:30am
CEA-TCB monotherapy: Clinical activity in mCRC
Radiological signs of tumor lesion inflammation seen at doses ≥60 mg

Data reported by investigators, cutoff: March 3, 2017. (safety data cut-off is ≥ 40 mg).
MMR=Mismatch repair status; DCR=Disease control rate (PR+SD); Tabernero J, et al. ASCO 2017, abstract #3002

Best change in target lesions from baseline (%)

<table>
<thead>
<tr>
<th>Best change in target lesions from baseline (%)</th>
<th>60 mg</th>
<th>90 mg</th>
<th>100 mg</th>
<th>135 mg</th>
<th>200 mg</th>
<th>300 mg</th>
<th>400 mg</th>
<th>600 mg</th>
<th>MMR unknown</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Confirmed best overall response RECIST v1.1</th>
<th>N=31; (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>2 (6.0%)</td>
</tr>
<tr>
<td>SD</td>
<td>12 (39%)</td>
</tr>
<tr>
<td>DCR</td>
<td>14 (45%)</td>
</tr>
<tr>
<td>PD</td>
<td>16 (52%)</td>
</tr>
<tr>
<td>Non-evaluable</td>
<td>1 (3.0%)</td>
</tr>
</tbody>
</table>
Dose-dependent clinical activity of CEA-TCB in combination with Tecentriq in mCRC

**Change in target lesions from baseline (%)**
*All patients N=25, 5-160 mg*

![Graph showing change in target lesions from baseline for different doses of CEA-TCB.]

**Confirmed best overall response RECIST v1.1**

<table>
<thead>
<tr>
<th>Response</th>
<th>N=25, 5 - 160 mg MSS n=23; (92%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>SD</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>DCR</td>
<td>13 (52%)</td>
</tr>
<tr>
<td>PD</td>
<td>12 (48%)</td>
</tr>
</tbody>
</table>

**Phase 1 combo data:**

- Clear correlation of CEA-TCB dose and response
- Promising clinical activity vs monotherapy in mCRC at doses ≥ 60 mg

Data reported by investigators, cutoff: March 3, 2017. *One patient had the confirmatory CT scan on March 23, 2017.* Sub-group of the column to the left (N = 25 CEA-TCB + Tecentriq patients, treated at doses 5 - 160 mg); DCR=Disease control rate (PR+SD) Tabernero J, et al. ASCO 2017, abstract #3002
CEA-TCB + Tecentriq: Promising clinical activity vs monotherapy in 3L+ MSS mCRC at high dose

**Change in target lesions from baseline (%)**

*High dose only, N=11, 80 or 160 mg*

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
<th>14</th>
<th>16</th>
<th>18</th>
<th>20</th>
<th>22</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 mg</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>160 mg</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Change in target lesion over time**

- **Withdrawal**
- **Progression**
- **Ongoing**
- **First new lesion**

**Confirmed best overall response RECIST v1.1**

<table>
<thead>
<tr>
<th></th>
<th>N=25, 5 - 160 mg MSS n=23; (92%)</th>
<th>N=11, 80 or 160 mg MSS n=11; (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>3(^a) (12%)</td>
<td>2(^a) (18%)</td>
</tr>
<tr>
<td>SD</td>
<td>10 (40%)</td>
<td>7 (64%)</td>
</tr>
<tr>
<td>DCR</td>
<td>13 (52%)</td>
<td>9 (82%)</td>
</tr>
<tr>
<td>PD</td>
<td>12 (48%)</td>
<td>2 (18%)</td>
</tr>
</tbody>
</table>

**Conclusions phase I studies:**

- Encouraging anti-tumor activity in heavily pre-treated patients with MSS mCRC
- Clinical activity seen with monotherapy; further enhanced in combo with Tecentriq
- Safety profile manageable in both monotherapy and in combination

Data reported by investigators, cutoff: March 3, 2017. \(^a\) One patient had the confirmatory CT scan on March 23, 2017. \(^b\) Sub-group of the column to the left (N = 25 CEA-TCB + Tecentriq patients, treated at doses 5 - 160 mg). Tabernero J, et al. ASCO 2017, abstract #3002
### CEA-TCB is the first T cell engaging therapy to show activity in solid tumors

#### Engineered T cells (CAR Ts)
- High interest, outstanding clinical efficacy with CD19 CARs in **hematology**
- Activity associated with high **toxicity**
- **Challenging manufacturing and regulatory processes**
- Applicability in **solid tumors**

#### T cell engaging bispecific antibodies

<table>
<thead>
<tr>
<th>Format</th>
<th>Potency</th>
<th>Long half-life</th>
<th>Differentiation of high vs low antigen expressing cells</th>
<th>Applicability in solid tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>BITE</td>
<td>✔️ ✔️ ✔️</td>
<td>✗</td>
<td>✔️</td>
<td>✗</td>
</tr>
<tr>
<td>“1:1” format</td>
<td>✔️</td>
<td>✔️ ✔️ ✔️</td>
<td>✔️</td>
<td>✗</td>
</tr>
<tr>
<td>“2:1” format</td>
<td>✔️ ✔️ ✔️</td>
<td>✔️ ✔️ ✔️</td>
<td>✔️</td>
<td>✔️ ✔️ ✔️</td>
</tr>
</tbody>
</table>

- **Italics** indicate notable features.
CEA-TCB: Potential to be efficacious in broad range of CEA-expressing solid tumors and to expand the benefit of CIT to more patients

Proportion of patients that are CEA\textsuperscript{High}

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal cancer</td>
<td>91%</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>74%</td>
</tr>
<tr>
<td>Gastric cancer</td>
<td>64%</td>
</tr>
<tr>
<td>NSCLC adeno</td>
<td>64%</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>29%</td>
</tr>
</tbody>
</table>

Clinical activity in mCRC enables a fast-to-market pathway
On completion of dose escalation, pivotal plans will be developed

CEA high = tumors expressing CEA in at least 20% of tumor cells with IHC 2+ and/or 3+
Bringing innovation to patients

Daniel O’Day
CEO Roche Pharmaceuticals
Our innovation strategy remains unchanged

Innovation & productivity supported by data analytics

Pipeline & commercial delivery

- Differentiated NMEs & strategic life-cycle mgmt.
- Commercial delivery

Data & analytics

- Smart, more efficient R&D
- Access & personalized patient care

Increased productivity

- Innovative trial design
- Prioritization & improved decision-making

Outstanding talent that drives innovation & execution

NME=new molecular entity
Innovation driving growth
*Focusing on areas with high unmet medical need*

Growing the existing business

... by improving Standard of Care

Expanding the business

... through advanced diagnostics and differentiated medicines
Breast: Raising the bar in HER2+
*Herceptin SC, Kadcyla & Herceptin/Perjeta combo*

---

**BC incidence rate**

- 66% HR+/HER2-
- 21% HER2+
- 13% TNBC

---

**Years**

11 12 13 14 15 16 17 18 19

---

**Adjuvant BC**

- Herceptin + chemo
- Herceptin SC + chemo (HannaH)
- Herceptin & Perjeta + chemo (APHINITY)

---

**Neoadj. BC**

- Herceptin + chemo (NOAH)
- Herceptin & Perjeta + chemo (Neosphere, Tryphaena)

---

**2 L mBC**

- Xeloda + lapatinib
- Kadcyla (EMILIA)

---

**1L mBC**

- Herceptin + chemo
- Herceptin + Perjeta + chemo (CLEOPATRA)

---

... and we will go further: combinations with Tecentriq in Phase I & II

1. Source: Datamonitor and internal estimates, US & EU5; SC=subcutaneous; BC=breast cancer
APHINITY to grow HER2 franchise

Strong value proposition in higher risk eBC patients

BC incidence rate\(^1\)

\[ \begin{array}{c}
\text{21\% HER2+} \\
\end{array} \]

HER2+ eBC (adj)

72k\(^{1,2}\)

\[ \begin{array}{c}
\text{Higher risk (Node+ ~55\%, HR- ~15\%, other higher risk ~5\%)}
\end{array} \]

\[ \begin{array}{c}
\sim 75\%
\end{array} \]

New standard of care for higher risk patients

1. Source: Datamonitor and internal estimates, US & EU5; 2. Target population for Herceptin in adjuvant breast cancer (US & EU5), current Herceptin penetration ~95%; eBC=early breast cancer; adj=adjuvant
Expanding to TNBC & HR+/HER2- BC
Areas with high unmet medical need

BC incidence rate¹

Ipatasertib: Identified PIK3CA/AKT1/PTEN-altered sub-population with increased benefit (LOTUS)

Ipatasertib + paclitaxel
Placebo + paclitaxel

Number at risk
Ipatasertib + pac 26 22 13 10 7 5 3 1 1
Placebo + pac 16 11 7 4 3 2 1

1. Source: Datamonitor and internal estimates, US & EU5; TNBC=triple negative breast cancer; HR=hormone receptor

FoundationOne key in identifying relevant patient sub-populations
Increasing efficacy through improved diagnostics

**LOTUS: PIK3CA/AKT1/PTEN-altered tumors**

**BC incidence rate**

- 66% HR+/HER2-
- 21% HER2+
- 13% TNBC

**TNBC**
- 1L: 23k\(^1,2\)

**HR+/HER2-**
- 1L: 88k\(^1,2\)

1. Source: Datamonitor and internal estimates, US & EU5; 2. Target population (US & EU5);
TNBC=triple negative breast cancer; HR=hormone receptor
Lung: Expanding to areas with high medical need

Multiple solutions for a fragmented market

<table>
<thead>
<tr>
<th>Target</th>
<th>Combo</th>
<th>Trial</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L ALK+</td>
<td>Alecensa</td>
<td>ALEX</td>
<td>✔️</td>
</tr>
<tr>
<td>2/3L</td>
<td>Tecentriq</td>
<td>OAK</td>
<td>✔️</td>
</tr>
<tr>
<td>1L non-sq</td>
<td>Tecentriq+carbo/pac+-Avastin</td>
<td>IMpower150</td>
<td>2017</td>
</tr>
<tr>
<td>1L non-sq</td>
<td>Tecentriq+carbo+nab-pac</td>
<td>IMpower130</td>
<td>2018</td>
</tr>
<tr>
<td>1L non-sq</td>
<td>Tecentriq+cis/carbo+pem</td>
<td>IMpower132</td>
<td>2018</td>
</tr>
<tr>
<td>1L Dx+</td>
<td>Tecentriq</td>
<td>IMpower110</td>
<td>2019</td>
</tr>
<tr>
<td>Adj</td>
<td>Tecentriq</td>
<td>IMpower010</td>
<td>2020</td>
</tr>
<tr>
<td>1L sq</td>
<td>Tecentriq+carbo+nab/pac</td>
<td>IMpower131</td>
<td>2018</td>
</tr>
<tr>
<td>1L SCLC</td>
<td>Tecentriq+carbo+etoposide</td>
<td>IMpower133</td>
<td>2018</td>
</tr>
</tbody>
</table>

1. Source: Datamonitor and internal estimates, US & EU5; 2. Timelines may change
Expanding CIT to difficult to treat tumors

**CEA-TCB**: Diagnostics to identify CEA\(^{\text{high}}\) patients

### Tumor Types and CEA\(^{\text{high}}\) Patients

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Statistics</th>
<th>CEA(^{\text{high}}) Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>1L: 149k(^2)</td>
<td>91%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1L: 57k(^2)</td>
<td>74%</td>
</tr>
<tr>
<td>Gastric(^3)</td>
<td>1L: 59k(^2)</td>
<td>64%</td>
</tr>
<tr>
<td>NSCLC(^4)</td>
<td>1L: 76k(^2)</td>
<td>64%</td>
</tr>
<tr>
<td>Breast</td>
<td>1L: 130k(^2)</td>
<td>29%</td>
</tr>
</tbody>
</table>

1. CEA = carcinoembryonic antigen, TCB = T-cell bispecific;  
2. Source: Datamonitor and internal estimates, US & EU5; equals target population;  
3. Adenocarcinomas and site stomach, lower/abdominal esophagus;  
4. NSCLC=non-small cell lung cancer adenocarcinoma population accounts for ~50% of all lung incidences
Industry leading portfolio of targeted & CIT assets
Maximizing value of our assets through combinations

CIT=Cancer Immunotherapy; Venclexta in collaboration with AbbVie; Gazyva in collaboration with Biogen; Alecensa in collaboration with Chugai; Cotelic in collaboration with Exelixis; Zelboraf in collaboration with Plexikon; polatuzumab in collaboration with Seattle Genetics; ipatasertib in collaboration with Array Biopharma; IDOi in collaboration with NewLink; daratumumab in collaboration with Janssen (J&J)
Status June 2017
Our innovation strategy remains unchanged

**Innovation & productivity supported by data analytics**

- **Pipeline & commercial delivery**
  - Differentiated NMEs & strategic life-cycle mgmt.
  - Commercial delivery

- **Data & analytics**
  - Smart, more efficient R&D
  - Access & personalized patient care

- **Increased productivity**
  - Innovative trial design
  - Prioritization & improved decision-making

---

Outstanding talent that drives innovation & execution
Agile & efficient development will be key

Driving speed and flexibility in clinical operations

Increasing speed

... through improved internal prioritization & resourcing

Driving flexibility

... through smart trial design and execution
JEWEL (Joint Effort to Win b/w Early and Late stage)
Internal “BTD” to accelerate key molecules

5 JEWEL molecules in oncology:
fit-for-purpose strategy and program acceleration

aCEA-TCB
Undisclosed
Undisclosed

aCD20-TCB
Undisclosed

Identified potential launch acceleration of up to 2 years

BTD=Breakthrough Therapy Designation
Agility and productivity in R&D

**MORPHEUS as novel CIT platform to drive combos**

MULTI-INDICATION

- NSCLC
- Pancreatic
- Gastric
- HR+ BC
- TNBC
- CRC
- UBC

MULTI-BASKET

- 1L
- 2L
- Biomarker

RANDOMIZED

- Combo 1
- Combo 2
- Combo 3

LONGLITUDINAL

- Soc control

ADAPTABLE

- Combo 4
- Combo 5
- Combo 6

Faster and more flexible decision-making AND potential for acceleration

CIT=Cancer Immunotherapy; SOC=standard of care
Our innovation strategy remains unchanged

Innovation & productivity supported by data analytics

Pipeline & commercial delivery

- Differentiated NMEs & strategic life-cycle mgmt.
- Commercial delivery

Data & analytics

- Smart, more efficient R&D
- Access & personalized patient care

Increased productivity

Cost

Quality

Speed

Outstanding talent that drives innovation & execution
Investing in advanced analytics technologies
... to improve R&D efficiency & patient care

Leveraging real world data ...
... to drive R&D productivity and Access

Focusing on next generation diagnostics & biomarker analytics ...
... to enhance personalized patient care
Summary: committed to our innovation strategy

Six launches in 2 years

Leading industry with 15 BTDs, 5 of 6 recent launches awarded a BTD
Doing now what patients need next