Bryan Garnier Oncology Day - Conference Call

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Introduction “Roche in oncology”

Overview “Cancer immunotherapy”

ASCO 2020 highlights: First anti-TIGIT (tiragolumab) data and lung cancer franchise update

Breast cancer franchise: HR+/HER2- and TNBC strategy

Hematology franchise: Venclexta, Polivy, glofitamab and mosunetuzumab

Outlook

Q&A
## Replace and extend the business: Q1 update

### Replace/extend existing businesses

<table>
<thead>
<tr>
<th>Category</th>
<th>Products/Drugs</th>
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<tbody>
<tr>
<td>MabThera/Rituxan</td>
<td>Gazyva, Venclexta, Polivy, mosunetuzumab, glofitamab</td>
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<td>Herceptin</td>
<td>Perjeta, Kadcyla, Perjeta+Herceptin FDC-SC</td>
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<td>Avastin</td>
<td>Tecentriq, Alecensa, Rozlytrek, ipatasertib</td>
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<td>Lucentis</td>
<td>faricimab, Port delivery system (PDS)</td>
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<td>Tamiflu</td>
<td>Xofluza</td>
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### Entering new franchises

**Oncology:**
- Gazyva, Tecentriq (mUC, HCC, melanoma)

**MS:**
- Ocrevus

**Hemophilia A:**
- Hemlibra

**CNS:**
- satralizumab (NMOSD), risdiplam (SMA), tominersen (Huntington’s), Autism, Alzheimer’s

**Immunology:**
- etrolizumab (UC, CD), Gazyva (lupus nephritis)

### Achievements Q1 2020

**Ocrevus:** US/EU: Short infusion filed

**risdiplam:**
- FIREFISH (SMA) part 2 meets primary endpoint in Type 1 patients
- SUNFISH (SMA) part 2 meets primary endpoint in Type 2 and 3 patients
- tominersen: GENERATION HD1 (Huntington’s) enrolled

### Replace/extend existing businesses

**Gazyva+Ven:**
- EU: Approval in 1L CLL

**Polivy:**
- EU: Approval in r/r DLBCL

**Venclexta:**
- Overall survival benefit in 1L AML

**Oncology:**
- Tecentriq (mUC, HCC, melanoma)

**MS:**
- Ocrevus

**Hemophilia A:**
- Hemlibra

**CNS:**
- satralizumab (NMOSD), risdiplam (SMA), tominersen (Huntington’s), Autism, Alzheimer’s

**Immunology:**
- etrolizumab (UC, CD), Gazyva (lupus nephritis)

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FDC=fixed dose combination; mUC=metastatic urothelial carcinoma; HCC=hepatocellular carcinoma; NMOSD=neuromyelitis optica spectrum disorder; SMA=spinal muscular atrophy; UC=ulcerative colitis; CD=Crohn’s disease; r/r DLBCL=diffuse large B-cell lymphoma; CLL=chronic lymphocytic leukemia; AML=acute myeloid leukemia; OS=overall survival; SCLC=small cell lung cancer; NSCLC=non-small cell lung cancer
Q1 2020: Oncology in line with previous year

YoY CER growth

HER2 franchise
- Kadcyla and Perjeta with strong global uptake in adjuvant BC

Avastin franchise
- Biosimilar erosion in US and Japan

Hematology franchise
- Venclexta:* Strong growth in 1L AML and 1L CLL
- Gazyva: Growth in 1L CLL and 1L FL
- Polivy: Strong US launch in R/R DLBCL

Tecentriq
- Growth driven by first-in-class launches in 1L SCLC & 1L TNBC

Alecensa
- Market leader in 1L ALK+ NSCLC; strong growth in China following NRDL listing

CER=Constant Exchange Rates; Q1 2020 Oncology sales: CHF 6.6bn; CER growth +0.45%; * Venclexta sales booked by AbbVie and therefore not included; BC=breast cancer; AML=acute myeloid leukemia; CLL=chronic lymphocytic leukemia; FL=follicular lymphoma; R/R DLBCL=relapsed/refractory diffuse large B cell lymphoma; SCLC=small cell lung cancer; TNBC=triple negative breast cancer; NSCLC=non-small cell lung cancer; NRDL=national reimbursement drug list
HER2 franchise: Perjeta and Kadcyla exceeding Herceptin sales

HER2 franchise Q1 update

- Perjeta (+22%): Global growth driven by eBC (APHINITY) and early uptake in China
- Kadcyla (+55%): Growth in adjuvant setting for patients with residual disease (KATHERINE); switching as planned
- Herceptin (-24%): Decline due to switching to Kadcyla and biosimilar erosion in the US

Outlook 2020

- Global Perjeta and Kadcyla uptake in eBC including China
- Accelerated Herceptin erosion in the US
- US approval for PH FDC SC (FeDeriCa)

CER=Constant Exchange Rates; eBC=early breast cancer; PH=Perjeta+Herceptin; FDC=fixed dose combination; SC=subcutaneous
Hematology franchise: Growth from Venclexta, Gazyva and Polivy

Hematology franchise Q1 update

CD20 franchise

- MabThera/Rituxan (-14%): Biosimilar erosion in the US
- Gazyva (+49%): Growth driven by 1L CLL (CLL14) and 1L FL

Venclexta*

- Strong growth driven by 1L unfit AML and 1L CLL (CLL14)
- Positive Ph III results for V+azacitidine in 1L unfit AML (Viale-A)

Polivy

- US: Uptake in 3L+ DLBCL and as CAR-T bridging therapy

Outlook 2020

- Strong growth of new products and on-going Rituxan erosion
- Updates on the CD20 x CD3 program and Polivy combinations

CER=Constant Exchange Rates; * Venclexta in collaboration with AbbVie; Gazyva in collaboration with Biogen; Polivy in collaboration with Seattle Genetics; CLL=chronic lymphocytic leukemia; FL=follicular lymphoma; AML=acute myeloid leukemia; DLBCL=diffuse large B cell lymphoma
Tecentriq overview: Q1 Growth driven by first-in-class indications
1L HCC approved in US on June 2; Filed in EU and China

Tecentriq Q1 update

Lung franchise (NSCLC, SCLC)
- US/EU/Japan: Growth driven by 1L SCLC and 1L NSCLC
- China: Approval in 1L SCLC achieved

Breast franchise (TNBC)
- US/EU: Growth driven by 1L PDL1+ TNBC

Outlook 2020
- US: First-in-class approval in 1L HCC achieved on June 2nd
- EU/China: First-in-class filing/approval in 1L HCC
- US: First-in-class filing/approval in 1L BRAF+ melanoma
- Ph III results in FL OC
- Ph III results in the (neo)adjuvant setting (TNBC, NSCLC)

CER=Constant Exchange Rates; SCLC=small cell lung cancer; NSCLC=non small cell lung cancer; TNBC=triple negative breast cancer; HCC=hepatocellular cancer; OC=ovarian cancer
COVID-19: Roche’s position in a rapidly changing environment

Limited timing impact on near-term launches and pivotal readouts

• **Major launches in 2020 on track:**
  1. Risdiplam (SMA type1/2/3)
  2. Satralizumab (NMOSD)
  3. PH FDC-SC (HER2+ BC)
  4. Tecentriq+Avastin (1L HCC)
  5. Venclexta+azacitidine (1L AML)

• **Pivotal readouts and pivotal trial starts in 2020 largely on track**

• **General remarks on on-going studies (things to watch):**
  • Clinical studies in oncology seem overall less impacted
  • We are continuously monitoring our on-going studies in chronic diseases, both in terms of missed doses and overall data integrity
  • Development teams are taking extraordinary efforts to protect these studies with continued support by the health authorities, especially the FDA
  • The ultimate impact will also depend on the length and severity of the pandemic
Introduction “Roche in oncology”

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ASCO 2020 highlights: First anti-TIGIT (tiragolumab) data and lung cancer franchise update

Breast cancer franchise: HR+/HER2- and TNBC strategy

Hematology franchise: Venclexta, Polivy, glofitamab and mosunetuzumab

Outlook

Q&A
Establishing Tecentriq as standard of care in major tumor types

1. Checkpoint Inhibitors Monotherapy
   Tecentriq in NSCLC: Impower110

2. Combine with Existing Medications
   Tecentriq + chemo/ targeted therapies in SCLC, TNBC, ovarian, HCC, bladder, etc.

3. Expand to novel CITs
   Immune doublets: Tecentriq + Bi-specifics, tiragolumab, etc.

4. Personalized CIT, RNAseq, etc.
   Combos/ NMEs: defined immune profiles

Wave 2
Tecentriq + Avastin in 1L HCC
Medically meaningful improvement

Wave 3
Tecentriq and tiragolumab in various cancer types have started Ph III development
- SKYSCRAPER-01 Ph III in PD-L1+ NSCLC
- SKYSCRAPER-02 Ph III in ES-SCLC
- SKYSCRAPER-04 Ph II in PD-L1+ cervical cancer

Wave 4
Tecentriq and tiragolumab in various cancer types have started Ph III development

- SKYSCRAPER-01 Ph III in PD-L1+ NSCLC
- SKYSCRAPER-02 Ph III in ES-SCLC
- SKYSCRAPER-04 Ph II in PD-L1+ cervical cancer

NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer; TNBC=triple-negative breast cancer; HCC=hepatocellular carcinoma
Strategies to promote an antitumor immune response by phenotype
Target “rate limiting steps” associated with primary and secondary resistance

Some patients may only require targeting of negative regulator (aPD–L1 monotherapy) to enable cancer immunity

Some patients will need two or more therapies to enable cancer immunity (e.g., to drive infiltration, boost MHC expression, etc)

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**ASCO 2020 highlights: First anti-TIGIT (tiragolumab) data and lung cancer franchise update**

Breast cancer franchise: HR+/HER2- and TNBC strategy

Hematology franchise: Venclexta, Polivy, glofitamab and mosunituzumab

Outlook

Q&A
There are many T cell checkpoints, including TIGIT

**Model for TIGIT regulation of T cell responses**

1. **Competition with CD226 for PVR**
   - PVR (CD155) competes with CD226 for PVR binding.

2. **Direct inhibition in cis**
   - TIGIT directly inhibits T cell activation in cis.

3. **Disrupts CD226 activation**
   - TIGIT disrupts CD226 activation.

**About TIGIT**

- **TIGIT** (T cell immunoreceptor with Ig and ITIM domains) is an inhibitory receptor, discovered at Genentech.
- TIGIT acts as a specific negative regulator of the CD226 costimulatory receptor.
- TIGIT is expressed on multiple immune cells, including CD8+ T cells (effector memory), CD4+ T cells (effector memory and regulatory), Tfh cells, and NK cells.
- TIGIT is expressed on a new population of T cells, stem-like memory cells, that may be the preferred targets for anti-PDx efficacy.

Johnson et al. Cancer Cell 2014
**Rationale for Tecentriq + TIGIT**

*PD1 and TIGIT are co-expressed on stem-like T-cells*

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**Anti-PD-L1 expands a key population of PD-1-positive T stem-like cells, which also express TIGIT but no other negative regulator**

- **T-cell expansion**
- **Prevent/reverse T-cell exhaustion**

Other potential MOA:
- Myeloid cell reprogramming
- T regulatory cell reprogramming
- NK effector function

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Modified from Chen and Mellman Nature 2017
An evolving paradigm: PD1/TIGIT blockade induce T cell expansion in draining lymph nodes to achieve therapeutic anti-tumor immunity
CITYSCAPE: Primary analysis of a randomized, double-blind, phase II study of the anti-TIGIT antibody tiragolumab plus Tecentriq versus placebo plus Tecentriq as 1L treatment in patients with PD-L1-selected NSCLC
CITYSCAPE rPh II: Tiragolumab plus Tecentriq in 1L NSCLC

Study design

1L Stage IV NSCLC
EGFR/ALK wild-type
Tumor PD-L1 TPS ≥ 1%
by 22C3 IHC by local or central assay
N=135

R 1:1

Tiragolumab 600 mg IV q3w +
Tecentriq 1200 mg IV q3w

Placebo 600 mg IV q3w +
Tecentriq 1200 mg IV q3w

No crossover

PD or loss of clinical benefit

- Co-primary endpoints: ORR and PFS in ITT
- Key secondary endpoints: Safety, DOR, OS
- Exploratory endpoints: Efficacy analysis by PD-L1 status

Stratification factors by baseline: ITT

<table>
<thead>
<tr>
<th></th>
<th>Tiragolumab + Tecentriq (n=67)</th>
<th>Placebo + Tecentriq (n=68)</th>
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<tbody>
<tr>
<td>Never used tobacco*</td>
<td>7 (10%)</td>
<td>7 (10%)</td>
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<tr>
<td>Non-squamous histology*</td>
<td>40 (60%)</td>
<td>40 (59%)</td>
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<tr>
<td>PD-L1 TPS ≥ 50%*</td>
<td>29 (43%)</td>
<td>29 (43%)</td>
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<tr>
<td>PD-L1 TPS 1-49%*</td>
<td>38 (57%)</td>
<td>39 (57%)</td>
</tr>
</tbody>
</table>

Primary data cut-off: 30 June, 2019; ITT=intention-to-treat; DOR = duration of response; IHC = immunohistochemistry; ORR = confirmed overall response rate; OS = overall survival; PD = progressive disease; PFS = progression free survival; q3w = every 3 weeks; R = randomized; TPS = tumor proportion score; *stratification factors
**CITYSCAPE rPh II: Tiragolumab plus Tecentriq in 1L NSCLC**

**Updated ORR analysis with 10.9 months median follow-up**

Consistent and clinically meaningful overall response rate (ORR), mainly driven by the PD-L1 high population (TPS>50%)

Follow-up data cut-off: 02 December, 2019; ITT=intention-to-treat; TPS=tumor proportion score
CITYSCAPE rPh II: Tiragolumab plus Tecentriq in 1L NSCLC
Updated PFS analysis with 10.9 months median follow-up

Updated investigator-assessed PFS: ITT

Updated Investigator-Assessed PFS: PD-L1 TPS ≥ 50%

Consistent and clinically meaningful PFS at longer follow-up with greater magnitude of improvement in the PD-L1 high population
Combining tiragolumab and Tecentriq was well-tolerated with similar rates of all Grade 3+ AEs compared with Tecentriq alone.
**CITYSCAPE: Immune-mediated adverse events (updated analysis)**

**Tiragolumab + Tecentriq (n=67)**

<table>
<thead>
<tr>
<th>Immune-Mediated Adverse Event*</th>
<th>n (%)</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>12 (18%)</td>
<td>46 (69%)</td>
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<tr>
<td>Infusion-Related Reactions</td>
<td>4 (6%)</td>
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<td>Pancreatitis (Lab)</td>
<td>2 (3%)</td>
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<tr>
<td>Hypothyroidism</td>
<td>1 (1%)</td>
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<tr>
<td>Hyperthyroidism</td>
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<tr>
<td>Colitis</td>
<td>1 (1%)</td>
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<tr>
<td>Diabetes Mellitus</td>
<td>1 (1%)</td>
<td></td>
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<tr>
<td>Ocular Inflammatory Toxicity</td>
<td>1 (1%)</td>
<td></td>
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<tr>
<td>Adrenal Insufficiency</td>
<td>1 (1%)</td>
<td></td>
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<tr>
<td>Nephritis</td>
<td>1 (1%)</td>
<td></td>
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<tr>
<td>Pneumonitis</td>
<td>1 (1%)</td>
<td></td>
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<tr>
<td>Hepatitis (Diagnosis and Lab)</td>
<td>1 (1%)</td>
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<tr>
<td>Myocarditis</td>
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<tr>
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**Placebo + Tecentriq (n=68)**

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<tbody>
<tr>
<td>Rash</td>
<td>9 (13%)</td>
<td>32 (47%)</td>
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<tr>
<td>Infusion-Related Reactions</td>
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<tr>
<td>Pancreatitis (Lab)</td>
<td>1 (1%)</td>
<td></td>
</tr>
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*immAE’s captured using Atezo AESI basket strategy to identify possibly immune related PT’s

More frequent immune-related AEs with the combination of tiragolumab and Tecentriq, but primarily Grade 1-2 IRR and rash

Updated data cutoff: 2 Dec 2019
**CITYSCAPE: Conclusions**

- Tiragolumab + Tecentriq showed clinically meaningful improvement in ORR and PFS in the ITT population compared to placebo + Tecentriq
- With longer follow-up, the treatment benefit of tiragolumab + Tecentriq remained consistent, with a greater magnitude of improvement seen in the PD-L1 TPS ≥ 50% subgroup
- Tiragolumab + Tecentriq was well-tolerated, with a safety profile similar to placebo + Tecentriq
  - Immune-mediated adverse events (imAEs) were more frequent with tiragolumab + Tecentriq but were primarily Grade 1-2 imAEs (mostly IRR and rash) and were manageable
- The observed activity and safety of tiragolumab + Tecentriq is to be confirmed in an ongoing Phase III study (SKYSCRAPER-01) in first-line PD-L1 TPS ≥ 50% NSCLC (NCT04294810)
**Tiragolumab: Broad clinical development program**

*Further studies to be started over the course of next 12 months*

<table>
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<tr>
<th>Phase 1</th>
<th>GO30103</th>
<th>Solid tumors</th>
<th>Ongoing</th>
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<td>Phase 1</td>
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<td>R/R Multiple myeloma or NHL</td>
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<td>Phase 2</td>
<td>CITYSCAPE</td>
<td>Non-small cell lung cancer PD-L1 TPS ≥ 1%</td>
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<tr>
<td>Phase 3</td>
<td>SKYSCRAPER-01</td>
<td>Non-small cell lung cancer PD-L1 TPS&gt;50%</td>
<td>Data at ASCO 2020</td>
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<tr>
<td>Phase 3</td>
<td>SKYSCRAPER-02</td>
<td>Extensive stage small-cell lung cancer</td>
<td>Data from NSCLC cohort at AACR 2020</td>
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<td>Phase 2</td>
<td>SKYSCRAPER-04</td>
<td>Cervical cancer PD-L1-selected</td>
<td>FPI Q1 ‘20</td>
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<td>MORPHEUS GI cancer</td>
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<td>MORPHEUS pancreatic cancer</td>
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<td>MORPHEUS urothelial carcinoma</td>
<td>Ongoing</td>
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Signal-seeking in various tumor types ongoing; four additional phase 3 studies including chemo-free immune doublets to be initiated in 2020.
Alecensa in 1L ALK+ NSCLC (ALEX):
Greater than 60% of patients alive after 5 years

Stage IIIB/IV ALK+ NSCLC
- Treatment naive
- ECOG PS 0–2
- Central ALK testing by IHC

Alectinib 600 mg twice daily
Crizotinib 250 mg twice daily

5-year OS rate (ITT) of 62.5% independent of CNS metastases at BL

The updated analysis confirms the superior OS efficacy and tolerability of Alecensa in comparison to crizotinib

*Data cut-off 29 Nov 2019; ECOG = Eastern Cooperative Oncology Group; PS = performance status; IHC = immunohistochemistry; ITT=intention-to-treat; OS = overall survival; NR = not reached
Rozlytrek in adult patients with \textit{NTRK} fusion-positive solid tumors: Updated integrated analysis\textsuperscript{1}

Best individual response per BICR, by tumor type; N=74

- Cholangiocarcinoma (n=1)
- Neuroendocrine (n=4)
- Sarcoma (n=16)
- GI-other (n=1)
- Pancreatic (n=5)
- Breast (n=6)
- Gynecological (n=2)
- Salivary MASC (n=13)
- Thyroid (n=7)
- CRC (n=7)
- NSCLC (n=13)

Clinically meaningful responses and survival outcomes in \textit{NTRK}-fp solid tumors

- ORR 63.5%
- mPFS 11.2 mo
- mOS 23.9 mo

Systemic efficacy irrespective of presence or absence of CNS metastases at baseline

- ORR with 62.5%
- ORR without 63.8%

Strong intracranial efficacy in patients with CNS metastases at baseline

- Intracranial ORR 50.0%

Durable disease control

- DoR 12.9 months vs previous 10.4

May 29, 2020: Positive CHMP opinion for Rozlytrek in \textit{NTRK} fusion-positive solid tumors and ROS1-positive, advanced NSCLC in patients 12 years of age and older

\textsuperscript{1}Integrated analysis of phase 1/2 studies (ALKA-372-001, STARTRK-1, STARTRK-2; EudraCT 2012-000148-88; NCT02097810; NCT02568267); Patients with missing SLD percent change are excluded from the plot. SLD, sum of longest diameters. GI, gastrointestinal. CRC, colorectal cancer. NSCLC, non-small-cell lung cancer. MASC, mammary analogue secretry carcinoma.
### Broadest NSCLC portfolio with the potential for chemo-free combos

*Newly added tiragolumab complements activity of Tecentriq*

<table>
<thead>
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<th>NSCLC (NSq)</th>
<th>NSCLC (Sq)</th>
<th>SCLC</th>
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<tr>
<td><strong>Non-Driver</strong></td>
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<tr>
<td>PD-L1+</td>
<td>PD-L1-</td>
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<tr>
<td><strong>ALK</strong></td>
<td><strong>EGR</strong></td>
<td><strong>ROS</strong></td>
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<td>Neo-/ Adj</td>
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<td><strong>1L</strong></td>
<td>Alecansa</td>
<td>Tarceva ± Avastin</td>
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<tr>
<td>SKYSCRAPER-01</td>
<td>Tiragolumab + Tecentriq</td>
<td>IMpower110</td>
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<td>Tecentriq</td>
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<td>Avastin + CP</td>
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<td><strong>2L</strong></td>
<td>IMpower150</td>
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<tr>
<td>OAK, POPLAR, BIRCH</td>
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<tr>
<td></td>
<td>Tarceva</td>
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</tbody>
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*Tiragolumab + TCQ+chemo*

**Neo-/ Adj**
- Alecensa

**1L**
- Alecensa
- Tarceva ± Avastin
- Roxitrex
- Roxytrex

**2L**
- IMpower150

**SKYSCRAPER-01**
- Tiragolumab + Tecentriq

**SKYSCRAPER-02**
- Tiragolumab + TCQ+chemo

- IMpower133 approved in Japan

- IMpower132 approved in Japan
Tecentriq + Avastin new SOC in 1L HCC
First-in-class US approval achieved; Filed in EU and China

IMbrave150: Overall survival primary analysis

- Statistically significant and clinically meaningful improvement in both OS and PFS with Tecentriq + Avastin vs sorafenib in patients with unresectable HCC who had not received prior systemic therapy
- Tecentriq + Avastin may be a practice-changing treatment for patients with unresectable HCC who have not received prior systemic treatment

IMbrave150: Confirmed progression-free survival

- 6-mo OS rate: 85%
- 6-mo OS rate: 72%
- mOS: 13.2 mo (95% CI: 10.4, NE)
- 6-mo PFS rate: 55%
- mPFS: 6.8 mo (95% CI: 5.7, 8.3)
- 6-mo PFS rate: 37%
- mPFS: 4.3 mo (95% CI: 4.0, 5.6)

NE, not estimable; a assessed by IRF per RECIST 1.1.; b HR and P value were from Cox model and log-rank test and were stratified by geographic region (Asia vs rest of world, including Japan), AFP level (< 400 vs ≥ 400 ng/mL) at baseline and MVI and/or EHS (yes vs no) per IxRS. c The 2-sided P value boundary based on 161 events is 0.0033. Data cutoff, 29 Aug 2019; median survival follow-up, 8.6 mo.
### Overview CIT adjuvant program

*Liver cancer added, lung and breast studies starting to read out in 2020*

| TNBC | neoadjuvant | IMpassion 031
Tecentriq + nab-paclitaxel |
|------|-------------|----------------------|
| neoadjuvant + adjuvant | NCT02620280 (sponsor Fondazione Michelangelo)
Tecentriq + nab-paclitaxel + carboplatin |
| | NCT03281954 (sponsor NSABP/GBG)
Tecentriq + carboplatin + paclitaxel |
| adjuvant | IMpassion 030
Tecentriq + paclitaxel followed by AC followed by Tecentriq |
| HER2+ BC | neoadjuvant | IMpassion 050
H+P + chemo + Tecentriq / surgery / Tecentriq + chemo |
| NSCLC | neoadjuvant | IMpower 030
Tecentriq + platinum based chemo |
| adjuvant | IMpower 010
Tecentriq following adjuvant cisplatin based chemo |
| adjuvant | ALINA
Alecensa |
| HCC | adjuvant | IMbrave050
Tecentriq + Avastin |
| RCC | adjuvant | IMmotion 010
Tecentriq |
| SCCHN | adjuvant | IMvoke 010
Tecentriq |

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<th>2019</th>
<th>2020</th>
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<tr>
<td>Tecentriq Ph III (Roche supported)</td>
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</table>

**Legend:**
- **IA:** Indicates studies in the adjuvant setting.

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Introduction “Roche in oncology”

Overview “Cancer immunotherapy”

ASCO 2020 highlights: First anti-TIGIT (tiragolumab) data and lung cancer franchise update

Breast cancer franchise: HR+/HER2- and TNBC strategy

Hematology franchise: Venclexta, Polivy, glofitamab and mosunetuzumab

Outlook

Q&A
### Largest breast cancer portfolio

**Expanding beyond HER2+ breast cancer**

<table>
<thead>
<tr>
<th>HER2+ BC</th>
<th>HER2+/HER2- BC</th>
<th>TNBC</th>
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<tbody>
<tr>
<td>20%</td>
<td>65%</td>
<td>15%</td>
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<table>
<thead>
<tr>
<th>mAb</th>
<th>Small molecule</th>
<th>ADC</th>
<th>CPI</th>
<th>Bispecifics</th>
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<tbody>
<tr>
<td>Herceptin</td>
<td>[Image]</td>
<td>[Image]</td>
<td>RG6194 (HER2/CD3)</td>
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<tr>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
<td>[Image]</td>
</tr>
</tbody>
</table>

- **mAb=monoclonal antibody; ADC=antibody drug conjugate; CPI=checkpoint inhibitor; TNBC=triple negative breast cancer; Venclexta in collaboration with Abbvie**

- **HER2+ BC**
  - Herceptin
  - [Image]

- **HR+/HER2- BC**
  - ipatasertib (AKT拮)
  - GDC-0077 (PI3K拮)
  - GDC-9545 (SERD拮)

- **TNBC**
  - ipatasertib (AKT拮)
  - TECENTRIQ [Image]

---

- [Image] = approved
TNBC treatment landscape

TNBC is not one disease, but a constellation of diseases

**Historical standard of care**

1L mBC
- Chemotherapy

TNBC patients defined by lack of actionable targets

**2020 (PHC approach)**

- BRCAm 15%
- PI3K/AKT/PTENm 35%
- PD-L1+ 40%

Treatment algorithm defined by relevant biomarkers

**Future (NME combinations)**

- All-comers benefit observed with Tecentriq + ipatasertib combination

- Tecentriq + chemo IMpassion130 1L TNBC (PD-L1+)
- Tecentriq + chemo IMpassion131 1L TNBC (PD-L1+)
- Tecentriq + chemo IMpassion132 1L TNBC (PD-L1+)
- ipatasertib + chemo IPATUNITY130 1L TNBC (PI3K/AKT/PTENm)
- ipatasertib + Tecentriq + chemo IPATUNITY170 1L TNBC

• Tecentriq is the first new agent approved in TNBC in ~15 years

TNBC=triple negative breast cancer; mBC = metastatic breast cancer; PHC = personalized healthcare; NME = new molecular entity
PIK3CA/AKT/PTEN includes any of the three mutations
SERDi (RG6171/GDC-9545) in HR+/HER2- mBC
Potentially best in class SERD to go straight into Ph III

Ph Ib results alone or combined with palbociclib

- RG6171: Superior drug metabolism and PK results in efficacy at low doses in vivo with wide nonclinical safety margins
- RG6171 is well-tolerated; Strong efficacy as a single agent or in combination in pre-treated ER+ mBC patients, regardless of ESR1 mutation status
- Further evaluation is underway assessing safety/efficacy at 30 mg daily in an expansion cohort given the promising anti-tumor effects with CBR of 50% and a safety profile observed at this dose level with no bradycardia events
- Ph III combination studies in HR+/HER2- mBC to be initiated
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Outlook

Q&A
### Broadest portfolio in hematology

<table>
<thead>
<tr>
<th></th>
<th>mAb</th>
<th>Small molecule</th>
<th>ADC</th>
<th>Bispecifics</th>
<th>CPI</th>
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<td><img src="image3" alt="POLIVY" /></td>
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</table>

- **CLL** = Chronic lymphoid leukemia; **DLBCL** = Diffuse large B-cell lymphoma; **iNHL** = Indolent Non-Hodgkin's lymphoma; **AML** = Acute myeloid leukemia; **MM** = Multiple myeloma; **MDS** = Myelodysplastic syndrome; **CPI** = checkpoint inhibitor; *Venclexta in collaboration with AbbVie*

---

**Indications**
- **CLL** = Approved
- **iNHL/FL** = Approved
- **DLBCL** = Approved
- **AML** = Approved
- **MM** = Approved
- **MDS** = Approved
- **Non-Malignant** = Approved

- **Indications where Rituxan approved**:
  - CLL
  - iNHL/FL
  - DLBCL
  - AML
  - MM
  - MDS

- **New hematologic diseases**:
  - Crovalimab

---

**Checkmarks**
- ▶️ = approved
- ▶️ = Indications where Rituxan approved
- ▶️ = New hematologic diseases
Roche combination regimens are improving efficacy and tolerability

**CLL**
- *Rituxan (Rituximab)* + chemo (chlorambucil)
- *GAZYVA obinutuzumab* + chemo
- *GAZYVA obinutuzumab* + *Venclexta*

**iNHL**
- *Rituxan (Rituximab)* + chemo (CHOP, CVP, benda)
- *GAZYVA obinutuzumab* + chemo
- *GAZYVA obinutuzumab* + glofitamab

**DLBCL**
- *Rituxan (Rituximab)* + chemo (1L: CHOP) (R/R: benda, gem-ox)
- *GAZYVA obinutuzumab* + *POLIVY* + chemo
- *POLIVY* + mosunetuzumab

**AML**
- chemo (1L unfit: HMA, LDAC)
- *Venclexta* + chemo
- *Venclexta* + idasanutlin

---

CLL=Chronic lymphoid leukemia; DLBCL=Diffuse large B-cell lymphoma; iNHL=Indolent Non-Hodgkin's lymphoma; AML=Acute myeloid leukemia; HMA = hypomethylating agents; LDAC = low dose cytarabine; Venclexta in collaboration with AbbVie
Innovation and acceleration of our portfolio

Develop novel endpoints

**Venclexta + Gazyva (CLL14)**

- MRD-negativity predictive of longer term benefit across several CLL and NHL trials

Innovative trial design

**Hemlibra (HAVEN2)**

- Intrapatient comparison trial demonstrated by Hemlibra has become gold standard in Hemophilia A trials

Fast to market development

**Venclexta + HMAs/LDAC (AML)**

- Venclexta granted accelerated approval in 1L AML on PhIb/II data
- Polivy launched of Ph 2 data (3 years ahead of projected timelines)

CLL=Chronic lymphoid leukemia; NHL=Non-Hodgkin’s lymphoma; AML=Acute myeloid leukemia; MRD=Minimal residual disease; HMA=hypomethylating agent; LDAC=low dose cytarabine; Venclexta in collaboration with AbbVie
High unmet need remains in DLBCL

**Challenges with CAR-T therapy**

- **Long timelines**: median 30-60 day wait, PD can occur\(^1\)
- **Toxicity**: risk of severe CRS, neurotoxicities
- **Cost**: high price, additional inpatient costs
- **Manufacturing**: 1-7% failure rate\(^2\)
- **Access**: administered only at specialist centers

**Roche portfolio in DLBCL**

- mosunetuzumab
- glofitamab

- Readily available “off the shelf”
- Well tolerated, with mAb dosing/PK properties
- Administered in outpatient facility

CAR-T therapies are a unique modality available for a small proportion of patients; high unmet need remains across NHL

Roche molecules have the potential for use in early lines of therapy including in combination therapy

---

CAR-T=chimeric antigen receptor T-cell; CRS=cytokine release syndrome; TCB = t-cell bispecific; DLBCL = diffuse large b-cell lymphoma; mAb = monoclonal antibody

\(^1\) Kymriah SMPC, Yescarta SMPC, Paillassa ASH 2019  
\(^2\) Neelapu NEJM 2018; Schuster NEJM 2019
Glofitamab (CD20 x CD3) in R/R NHL
Ph I dose escalation update to be presented at EHA (June 12)

Glofitamab in R/R aNHL (PhI dosing): Strong efficacy and tolerable safety

10-16 mg cohorts*: ORR 19/33 (58%); CR 13/33 (39%)

Clinical case
• DLBCL patient with 6 prior lines: R-CHOP 21 (CR), R-DHAOX (SD), Selinexor (PD), GemOx-nivolumab (PD), lenalidomide plus RT (SD) and bromodomain inhibitor (PD)
• CR after 6 doses of CD20-TCB (16mg), surgical removal of necrotic PET-negative crust on Mar 14

Dickinson, M., et al, ICML 2019; R/R=relapsed/refractory; NHL=non-Hodgkin’s lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine, prednisone; R=Rituxan; OR=overall response; CR=complete response; SD=stable disease; PD=progressive disease; CRS=cytokine release syndrome; AE=adverse event; *aNHL includes FL Grade 3B, DLBCL, trFL, PMBCL, MCL, trMZL, RS and DLBCL/MCL

• Ph I dose escalation update to be presented at EHA on June 12
• Ph III of glofitamab + gem-ox vs Rituxan + gem-ox in R/R DLBCL initated
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Outlook

Q&A
**2020: Key late-stage news flow**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Indication</th>
<th>Milestone</th>
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<tr>
<td><strong>Regulatory</strong></td>
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<tr>
<td>Rozytrek</td>
<td>NTRK pan tumor; ROS1 + NSCLC</td>
<td>EU approval</td>
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<tr>
<td>Venclexta + Gazyva</td>
<td>1L unifit CLL</td>
<td>EU approval</td>
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<tr>
<td>Polivy + Rituaxan + chemo</td>
<td>IV/R DLBCL</td>
<td>EU approval</td>
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<td>risdiplam</td>
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<td>NMOSD</td>
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<td>Nasal polyps</td>
<td>US approval</td>
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<td>1L BRAF+ Melanoma</td>
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<td>Tecentriq + Avastin</td>
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<td>Tecentriq</td>
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<td>Autism spectrum disorder</td>
<td>Ph III Viaduct/Ph II aVition $\times\times$</td>
</tr>
</tbody>
</table>

**Additional 2020 news flow:**

- **Actemra:** Ph III start in hospitalised patients with severe COVID-19 pneumonia (results expected end of June)
- **Actemra + remdesivir:** Ph III start in hospitalised patients with severe COVID-19 pneumonia

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* Outcome studies are event-driven: timelines may change; ** Ph III in adults negative; Ph II in pediatrics ongoing
Q&A

Doing now what patients need next