Roche Pharma Day 2019

Late Stage Pipeline Oncology

Sandra Horning | Chief Medical Officer and Head Global Product Development
Late stage pipeline update

Topics covered in presentations and break-out sessions

1. Hematology franchise
   - CLL: Venclexta Gazyva
   - DLBCL: Polivy, Venclexta
   - NHL, DLBCL: mosunetuzumab, CD20xCD3
   - AML: Venclexta, idasanutlin
   - MM: Venclexta

2. Breast Cancer franchise
   - HER2+: Kadcyla, Perjeta, FDC SC, Tecentriq
   - TNBC: Tecentriq, ipatasertib
   - HR+: ipatasertib; PI3Kα inhibitor; SERD

3. Lung Cancer franchise
   - NSCLC: Tecentriq
   - ALK+: Alecensa
   - ROS1+/NTRK+: Rozlytrek

4. GU franchise
   - mUC: Tecentriq
   - CRPC: ipatasertib

5. Pan tumor
   - NTRK+ tumors: Rozlytrek

6. Other oncology
   - Melanoma: Tecentriq, Cotelpic, Zelboraf
   - OC: Tecentriq, Avastin
   - HCC: Tecentriq, Avastin

7. Neuroscience
   - MS: Ocrevus update
   - SMA: risdiplam
   - NMOSD: satralizumab
   - Huntington’s disease: HTT-ASO
   - Autism: balovaptan
   - Parkinson’s disease: prasinezumab

8. Infectious diseases
   - Influenza A/B: baloxavir marboxil

9. Immunology
   - Lupus nephritis: Gazyva
   - Ulcerative colitis: etrolizumab
   - Crohn’s disease: etrolizumab
   - Food allergy: Xolair
   - Nasal polyps: Xolair

10. Hemophilia A
   - Hemlibra

11. Pan tumor
   - NTRK+ tumors: Rozlytrek

12. Other oncology
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   - OC: Tecentriq, Avastin
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21. Neurology
   - MS: Ocrevus update
   - SMA: risdiplam
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* For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 18 results presentation appendix or visit the IR homepage.
### Oncology: Progress since late 2018

**12 pivotal studies addressing needs of >800k patients reading out soon**

#### Lead in Hematology
- **NHL**: Rituxan, Gazyva, Venclexta, Polivy, mosunetuzumab, CD20xCD3
- **CLL**: Venclexta, Gazyva
- **AML**: Venclexta, idasanutlin
- **MM**: Venclexta
- **Hemophilia A**: Hemlibra

#### Lead in Breast Cancer
- **HER2+ BC**: Herceptin, Perjeta, Kadcyla, H+P FDC SC
- **TNBC**: Tecentriq, ipatasertib
- **HR+ BC**: ipatasertib, PI3Kα inhibitor (RG6114); SERD (RG6171)

#### Growth in Lung
- **ALK+/ROS1+/NTRK+**: Alectinib, Rozlytrek
- **SCLC**: Tecentriq
- **NSCLC**: Tecentriq, Avastin

#### Establish presence (with Tecentriq and combos)
- **mUC**: Expand in 1L; Move into adjuvant
- **HCC**: Potential new SOC
- **CRPC**: Potential new SOC
- **OC**: Potential new SOC
- **RCC and CRC**: Explore opportunities

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- Digital table containing medical information.

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- Visual representation of lead indications per therapeutic area.

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- Diagram highlighting high medical need in later lines, aNHL and AML.

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- Chart illustrating progress since Pharma Innovation Day (September 2018).

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- Text boxes indicating significant progress.

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- Symbols for adjuvant treatment and metastatic patient rates.
Roche significantly advancing patient care
26 BTD’s reflecting the quality of our research

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<thead>
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<td>Kadryla</td>
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✓ = approved
## Acceleration of development timelines

**Aiming for more faster**

<table>
<thead>
<tr>
<th>Transformational data</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
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<td>Ph1b, Ph2</td>
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<tr>
<td>Polivy + BR in R/R DLBCL</td>
<td>3.0 y</td>
<td>Q2 2019</td>
<td>Q2 2022</td>
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<tr>
<td>Venclexta + azacitidine in 1L AML</td>
<td>2.8 y</td>
<td>Q4 2018</td>
<td>Q4 2021</td>
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<table>
<thead>
<tr>
<th>Innovative Trials</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
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<tbody>
<tr>
<td>Ph1b to Ph3</td>
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<tr>
<td>Tecentriq + chemo +/- Avastin in 1L NSCLC</td>
<td>2.5 y</td>
<td>Q4 2018</td>
<td>Q1 2022</td>
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<td>Tecentriq + chemo in 1L SCLC</td>
<td>2.5 y</td>
<td>Q1 2019</td>
<td>Q2 2022</td>
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<tr>
<td>Tecentriq + nab-paclitaxel in 1L TNBC</td>
<td>2.5 y</td>
<td>Q2 2019</td>
<td>Q3 2022</td>
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</tbody>
</table>

### Faster-Filing

- 2018: 21 weeks/filing (-5.4 weeks vs. ’17)
- Total of 25 filings = -2.6y saved
- Target 2019: 16 weeks/filing (-10.4w vs. ’17)
- Total of 20 filings = -4.0y saved

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Clinical trial combination screening platforms established in CIT and hematology
Late stage pipeline update

Topics covered in presentations and break-out sessions

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<td>• mUC: Tecentriq</td>
<td>• NTRK+ tumors: Rozlytrek</td>
<td>• Melanoma: Tecentriq, Cotellic, Zelboraf</td>
<td>• MS: Ocrevus update</td>
<td>• Lupus nephritis: Gazyva</td>
<td>• DME, nAMD: faricimab</td>
<td>• Oncology / Hematology</td>
</tr>
<tr>
<td>• DLBCL: Polivy, Venclexta</td>
<td>• TNBC: Tecentriq, ipatasertib</td>
<td>• ALK+: Alecensa</td>
<td>• CRPC: ipatasertib</td>
<td></td>
<td>• OC: Tecentriq, Avastin</td>
<td>• SMA: risdiplam</td>
<td>• Ulcerative colitis: etrolizumab</td>
<td>• AMD, nAMD: faricimab</td>
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<td>• NMOSD: satralizumab</td>
<td>• Crohn’s disease: etrolizumab</td>
<td>• AMD: Port Delivery System</td>
<td>• Ophthalmology</td>
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<td>• AML: Venclexta, idasanutlin</td>
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<td>• Food allergy: etrolizumab</td>
<td>• GA: ASO factor B</td>
<td>• Infectious diseases</td>
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<tr>
<td>• MM: Venclexta</td>
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<td>• Nasal polyps: Xolair</td>
<td>• Choroideremia: Gene therapy</td>
<td>• Immunology</td>
</tr>
</tbody>
</table>

* For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 18 results presentation appendix or visit the IR homepage
Uniquely positioned to improve SOC in hematology
Largest late stage portfolio allows to develop new combinations

Rituxan
Gazyva
Polivy
Venclexta
mosunetuzumab
CD20 x CD3 TCB
idasanutlin
Bcl2 inhibitor
Anti-CD79b
Anti-CD20
Anti-CD20 x Anti-CD3
MDM2 antagonist
Abs
Small molecule
Ab-drug conjugate
T cell bispecifics
Small molecule

developing combinations
developing combinations
developing combinations

7 molecules approved / late stage
5 different MOAs
4 different platform technologies
Hematology: Venclexta + Gazyva in 1L unfit CLL
Fast track approval following outstanding PFS and MRD data

Venclexta program

Ph III (CLL14) results:

Bcl-2 inhibitor

Minimal residual disease

<table>
<thead>
<tr>
<th>Combination</th>
<th>Indication</th>
<th>Ph1</th>
<th>Ph2</th>
<th>Ph3</th>
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<tr>
<td>V+R/G+Clb</td>
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<tr>
<td>V+R</td>
<td>DLBCL</td>
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<tr>
<td>V+pola+G/R</td>
<td>R/R DLBCL/FL</td>
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<tr>
<td>V+G</td>
<td>1L, DLBCL</td>
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<td>V+R</td>
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<tr>
<td>V</td>
<td>R/R CLL, 17p</td>
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<tr>
<td>V+G</td>
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<td>V+az</td>
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<table>
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<tr>
<th>MRD-negative, % bone marrow (95%CI)</th>
<th>V+G</th>
<th>G+Clb</th>
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<tr>
<td>PFS HR of 0.33 versus Gazyva + chlorambucil; mPFS not reached</td>
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<td>First fixed 12-month treatment, chemotherapy-free option</td>
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<td>Approval following 10 weeks after submission via the RTOR pilot program</td>
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Fischer K. et al., ASCO 2019; PFS=progression free survival; HR=hazard ratio; V=Venclexta; G=Gazyva; clb=chlorambucil; R=Rituxan; dex=dexamethasone; bor=bortezomib; T=Tecentriq; aza=azacitidine; LDAC=low dose cytarabine; RTOR=real-time oncology review; Venclexta in collaboration with AbbVie; Gazyva in collaboration with Biogen; Cotellic in collaboration with Exelixis
Hematology: Very strong US launch for Polivy
First approval for Polivy + BR in R/R DLBCL

Sehn L. H. et al., ASH 2018; ADC=antibody drug conjugate; DLBCL=diffuse large B-cell lymphoma; PFS=progression free survival; OS=overall survival; HR=hazard ratio; BR=bendamustine+Rituxan; 1. In R/R DLBCL patients not candidates for transplant; Polivy in collaboration with Seattle Genetics

- Rapid uptake in R/R DLBCL following early US approval; EU approval expected in 2H
- Safely administered in combination with BR; also used as an off-the-shelf bridge therapy to consolidative therapies
- Ph III (POLARIX) in 1L DLBCL fully recruited ahead of schedule; Ph III (POLARGO) with additional chemo combinations in R/R DLBCL initiated
**Hematology: CD20 x CD3 program in NHL**

**Strong durable efficacy and tolerable safety**

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**CD20 x CD3 program**

- **Mosunetuzumab (PhI dosing):**
  - **Induces durable CR in R/R indolent and aggressive NHL; CRs in patients refractory to R-CHOP and CAR-T**
  - **Favorable safety profile: Cycle 1 step-up dosing appears to mitigate toxicity**
  - **Dose optimization and combination trials with Tecentriq, Polivy and CHOP ongoing; Further efficacy update planned for H2 2019**

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**Hematology: CD20 x CD3 program**

**R/R aNHL**

- Median duration of CR not reached
- Median CR follow up: 298 days (46–816 days)

**R/R FL**

- Median duration of CR not reached
- Median CR follow up: 330 days (54–788 days)

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**Budde, L. et al, ASCO 2019; NHL=non-Hodgkin's lymphoma; mosun=mosunetuzumab; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine, prednisone; pola=polatuzumab; T=Tecentriq; G=Gazyva; R=Rituxan; CR=complete response; R/R=relapsed/refractory; SPD=sum of the product diameters; CAR T cells=chimeric antigen receptor; *includes R/R DLBCL/trFL**
Hematology: CD20 x CD3 program in NHL
Strong efficacy and tolerable safety

CD20 x CD3 (PhI dosing):

- Continues to show highly encouraging OR and CR rates in R/R indolent and aggressive NHL
- 10-16 mg dosing cohorts with ORR of 58% and a CRR of 39%
- Main safety signal is CRS: Mostly confined to cycle 1 and all but one patient was re-dosed at same dose level at cycle 2
- Overall low rate of AEs leading to discontinuation (1%)

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

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
**Hematology: Idasanutlin in AML**

**Promising activity in combination**

### Idasanutlin program

- **MDM2 antagonist**

![MDM2 antagonist structure](image)

### Ph III (MIRROS) trial design

- **R/R AML**
  - **Indication:**
    - Idasanutlin + cytarabine: R/R AML
    - Idasanutlin + V: unfit for chemo
    - Idasanutlin + cytarabine + dasatinib: 1L AML
    - Idasanutlin: Hydroxyurea resistant/ intolerant PV

- **Ph I/II/III**

### Ph III (MIRROS) trial design

- **R/R AML**
  - **Ph III**
    - **Combination:** Idasanutlin 300mg PO BID + cytarabine 1g/m² IV day 1-5 q28 days
    - **Indication:**
      - Idasanutlin + cytarabine: R/R AML
      - Idasanutlin + V: unfit for chemo
      - Idasanutlin + cytarabine + dasatinib: 1L AML
      - Idasanutlin: Hydroxyurea resistant/ intolerant PV

- **Positive interim analysis**
  - Efficacy and safety
  - 120 patients TP53 wild type
  - Performed by iDRC
  - High efficacy bar based on durable CR/EFS

- **1 EP:**
  - OS in TP53 wild type

- **2 EP:**
  - CR, ORR; EFS; Proportion of HSCT; PRO

- **Responding patients may receive optional consolidation with up to 2 additional cycles**

### Phases

- **Ph I**
  - In heavily pretreated AML patients: idasanutlin+cytarabine showed 29% cCR rate (all patients) and 42% cCR rate in patients dosed with Ph III dose with a mDoR >8m

- **Ph II** (NCT02670044): Venclexta+idasanutlin showed clinical activity (46% anti-leukemic RR and 33% CR+CRi+CRp rate at 600mg Venclexta + 150/200mg idasanutlin) in unfit R/R AML

- **Ph III** (MIRROS) in R/R AML is one of the largest R/R AML studies; NME filing possible in 2020

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Martinelli G, et al., EHA 2016; Daver N, et al., ASH 2018; OS=overall survival; cCR, leukemic RR (CR+CRp+CRi+MLFS); CR=complete remission rate; CRp=complete remission with incomplete platelet recovery; CRi=complete remission with incomplete count recovery, MLFS=morphologic leukemia-free state; mDoR=median duration of response; V=Venclexta; PV=polycythemia vera
Late stage pipeline update

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   - CLL: Venclexta, Gazyva
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   - MM: Venclexta

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   - HER2+: Kadcyla, Perjeta, FDC SC, Tecentriq
   - TNBC: Tecentriq, ipatasertib
   - HR+: ipatasertib; PI3Kα inhibitor; SERD

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   - ROS1+/NTRK+: Rozlytrek

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   - NMOSD: satralizumab
   - Huntington’s disease: HTT-ASO
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    - DME, nAMD: faricimab
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    - GA: ASO factor B
    - Choroideremia: Gene therapy

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TNBC franchise: Tecentriq + nab-pac new SOC in 1L
Additional near-term read-outs in neoadjuvant and 1L

Tecentriq+nab-pac: Ph III (IMpassion130)

- Clinically meaningful OS improvement (2nd interim) PDL1+ population
- Stratified HR = 0.71* (95% CI: 0.54, 0.94)
- Δ 7 mo
- Overall survival (%)
- Time (months)
- 18.0 mo (15.6, 20.1)
- 25.0 mo (19.6, 30.7)

TNBC program covering all lines of treatment*

- 1L PDL1+TNBC: Tecentriq+nab-pac new SOC; PFS showed a HR=0.62 with mPFS improving from 5.0m to 7.5m
- Ph III (IMpassion131): Results for Tecentriq+paclitaxel in 1L expected early 2020
- Ph III (IMpassion031): Results for Tecentriq+nab-pac in neoadjuvant expected in 2020

Schmid P, et al. ASCO 2019 (Data cutoff: January 2, 2019); Schmid P, et al. ESMO 2018; TNBC=triple negative breast cancer; nab-pac=nab-paclitaxel (Abraxane); HR=hazard ratio; OS=overall survival; *Not formally tested due to pre-specified hierarchical analysis plan (data included in the EMA label); *Outcome studies are event-driven: timelines may change
Ipatasertib in TNBC and HR+ mBC
Strong PFS and OS benefit in 1L TNBC; New Ph III trials initiated

Highly selective AKT inhibitor

- Oral, highly specific inhibitor of all three activated isoforms of AKT, blocking the PI3K/AKT signaling pathway and potentially preventing cancer cell growth and survival
- Clinical development in tumors with high frequency of PI3K/AKT pathway activation (TNBC, HR+ mBC, CRPC)

Phase II (LOTUS):

- PFS HR was 0.44 for Dx+ patients vs 0.6 for all-comers; OS trend with HR of 0.62 (all-comers)
- Positive Ph I data in 1L TNBC for ipatasertib+Tecentriq+chemo: 73% ORR in all-comers
- Ph III (IPATunity150) ipatasertib+fulvestrant+palbociclib in 1L HR+ mBC and Ph III (IPATunity170) ipatasertib+Tecentriq+chemo in 1L TNBC initiated
- Ph III (IPATunity130) results in Dx+ 1L TNBC and in Dx+ HR+/HER2- mBC expected in 2020

FMI NGS assay:

- Detects all classes of genetic alterations in 324 oncogenes + CIT biomarkers MSI and TMB
- 18 therapies currently approved for inclusion in the report

Dent R. et al., ASCO 2018; Schmidt P. et al, ACCR 2019; TNBC=triple negative breast cancer; HR=hormone receptor; BC=breast cancer; PFS=progression free survival; OS=overall survival; HR=hazard ratio; Ipatasertib in collaboration with Array BioPharma.
RG6114 in \textit{PIK3CA}-mutant HR+/HER2- mBC

Potentially best in class PI3K\(\alpha\) inhibitor to go straight into Ph III

Highly selective PI3K\(\alpha\) inhibitor

- Differentiation to previous PI3K inhibitors:
  - More selective for PI3K\(\alpha\)
  - Greater safety margins
  - Better in vivo efficacy
- Degrades mutant PI3K\(\alpha\)
- Greater, more durable target inhibition
- Combinations with standard therapies

Tumor growth inhibition as single agent or in combination

\textit{PIK3CA}-mutant breast cancer xenograft mouse models

- On-going Ph I/Ib to evaluate RG6114 as single agent in patients with locally advanced or metastatic \textit{PIK3CA}-mutant solid tumors and in combination with endocrine and targeted therapies in locally advanced or metastatic \textit{PIK3CA}-mutant HR+/HER2- breast cancer
- First Ph I/Ib data to be presented at upcoming conference
- Ph III study in 1L \textit{PIK3CA}-mutant HR+/HER2- mBC to start in 2019

Edgar K. \textit{et al.}, AACR 2017; HR=hormone receptor; BC=breast cancer
**RG6171 in HR+/HER2- mBC**

Potentially best in class SERD to go straight into Ph III

**Selective ER degrader (SERD)**

- 3rd generation molecule
- Highly potent in vitro and improved efficacy in vivo versus other SERDs
- Superior drug metabolism and PK results in efficacy at low doses in vivo
- High potency + minimal safety findings lead to wide nonclinical safety margins

**Tumor growth inhibition as single agent or in combination**

- **Tumor regression in wt and mutant ER+ xenograft mouse models**
- **Increased tumor growth inhibition in combination with CDK4/6 inhibitors**

- RG6171 causes ER degradation, tumor growth inhibition and enhances the efficacy of CDK4/6 inhibitors in xenograft mouse models
- Unlike tamoxifen and some previous SERDs no estrogenic activity in rodent uteri is seen
- Ph I/IIb data (+/-palbociclib or hormonal therapy) to be presented at upcoming conference
- Ph III combination studies in HR+/HER2- mBC to be initiated

Metcalf C. *et al.*, SABCS 2018; HR=hormone receptor; BC=breast cancer; ER=estrogen receptor; PK=pharmacokinetics
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   - Hemlibra

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NSCLC franchise: Tecentriq in 1L PDL1+ NSCLC

Positive results for Tecentriq monotherapy

**Ph III (IMpower110) trial design**

- **PDL1+ 1L NSq and Sq NSCLC chemo naive stage IV N=555**
- **R: 1:1**
- 4 or 6 x 21 day cycles NSq: carboplatin or cisplatin + pemetrexed
  Sq: carboplatin or cisplatin + gemcitabine
- 1 EP:
  - OS
  - (by PDL1 subgroups)
- 2 EP:
  - PFS
  - ORR
  - DOR

**followed by maintenance:**

- Tecentriq 1200mg q21d
- **OS follow up**
  - No cross-over allowed
- NSq: pemetrexed
  Sq: Best supportive care
  - Treatment until PD or loss of benefit

**NSCLC portfolio covering all segments**

- **Positive Ph III (IMpower110) results for Tecentriq monotherapy in 1L PDL1+NSCLC**
- **Data to be presented at ESMO**

NSq=non-squamous; Sq=squamous
NSCLC franchise: 1L ALK+/ROS1+/bTMB high NSCLC

Patient selection based on blood-based NGS ctDNA assays

Ph III trial design (B-FAST) for 1L treatment naive NSCLC

Blood based biomarkers:

- Only 17ml blood needed
- A single liquid biopsy test that detects the 4 main classes of genomic alterations (70 genes)
- Comprehensive genomic profile including resistance mutations or fusions in NSCLC
- Includes MSI status
- Guides therapy selection and clinical trials

Mok T. et al., WCLC 2017; NGS=next generation sequencing; ctDNA=circulating tumor DNA; RWD=real world data
NSCLC franchise: Rozlytrek in ROS1+ mNSCLC

Strong responses in patients with brain metastases

Selective NTRK/ROS1 inhibitor

- Selective, CNS-active inhibitor of ROS1/NTRK/ALK tyrosine kinases
- Activating ROS1 rearrangements occur in 1-2% of NSCLC
- Activating rearrangements in TRK have been identified in >17 different solid tumors, including head and neck, thyroid, sarcoma and brain

Integrated Ph I/II (ALKA, STARTRK-1/2) results:

Pivotal, open-label, multicenter, global, basket study

<table>
<thead>
<tr>
<th></th>
<th>Total n=53</th>
<th>CNS disease at baseline (n=23)</th>
<th>No CNS disease at baseline (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR (%) (95% CI)</td>
<td>41 (77.4) (63.8, 87.7)</td>
<td>17 (73.9) (51.6, 89.8)</td>
<td>24 (80.0) (61.4, 92.3)</td>
</tr>
<tr>
<td>Median DOR (months) (95% CI)</td>
<td>24.6 (11.4, 34.8)</td>
<td>12.6 (6.5, NE)</td>
<td>24.6 (11.4, 34.8)</td>
</tr>
<tr>
<td>Median PFS (months) (95% CI)</td>
<td>19.9 (12.2, 36.6)</td>
<td>13.6 (4.5, NE)</td>
<td>26.3 (15.7, 36.6)</td>
</tr>
</tbody>
</table>

- Ph1/II results in ROS1+ mNSCLC: 77% systemic ORR with 74% ORR in patients with CNS disease at baseline
- mDOR of 24.6m and mPFS of 19.0m
- Updated Ph II (ALKA, STARTRK-1/2) data in NTRK+/ROS1+ tumors to be presented at ESMO

Doebele RC. et al., WCLC 2018; ORR=overall response rate; mDOR=median duration of response; mPFS=median progression free survival
Overview CIT adjuvant program

*Lung, breast and bladder studies starting to read out in 2020*

<table>
<thead>
<tr>
<th>Disease</th>
<th>Phase</th>
<th>Study</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNBC</td>
<td>neoadjuvant</td>
<td>IMpassion 031</td>
<td>Tecentriq + nab-paclitaxel</td>
</tr>
<tr>
<td></td>
<td>neoadjuvant + adjuvant</td>
<td>NCT02820280 (sponsor Fondazione Michelangelo)</td>
<td>Tecentriq + nab-paclitaxel + carboplatin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NCT0328195A (sponsor NSABP/GBG)</td>
<td>Tecentriq + carboplatin + paclitaxel</td>
</tr>
<tr>
<td>HER2+ BC</td>
<td>adjuvant</td>
<td>IMpassion 030</td>
<td>Tecentriq + paclitaxel followed by AC followed by Tecentriq</td>
</tr>
<tr>
<td></td>
<td>neoadjuvant</td>
<td>IMpassion 050</td>
<td>H + P + chemo + Tecentriq / surgery / Tecentriq + chemo</td>
</tr>
<tr>
<td>NSCLC</td>
<td>neoadjuvant</td>
<td>IMpower 019</td>
<td>Tecentriq + platinum based chemo</td>
</tr>
<tr>
<td></td>
<td>adjuvant</td>
<td>IMpower 019</td>
<td>Tecentriq following adjuvant cisplatin based chemo</td>
</tr>
<tr>
<td></td>
<td>adjuvant</td>
<td>ALINA</td>
<td>Alecensa</td>
</tr>
<tr>
<td>MIBC</td>
<td>adjuvant</td>
<td>IMVigor 010</td>
<td>Tecentriq</td>
</tr>
<tr>
<td>RCC</td>
<td>adjuvant</td>
<td>IMmotion 010</td>
<td>Tecentriq</td>
</tr>
<tr>
<td>SCCHN</td>
<td>adjuvant</td>
<td>IMvolve 010</td>
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Late stage pipeline update

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GU franchise: Tecentriq in bladder cancer
Positive results for Tecentriq + chemo in 1L; Adjuvant data in 2020

Ph III (IMvigor130) trial design

- Positive Ph III (IMvigor130) results for Tecentriq+gemcitabine/carboplatin+cisplatin in 1L mUC to be presented at ESMO
- Phase III (IMvigor010) results for Tecentriq monotherapy in the adjuvant setting expected in 2020

Standard of care evolution in the US

MIBC=muscle invasive bladder cancer; mUC=metastatic urothelial cancer; Patient numbers (US+EU-5): Roche internal estimates; *Current 1L approval is for cis-ineligible PD-L1+ (EU/US) and platinum-ineligible (US)
GU franchise: Ipatasertib in 1L mCRPC

**Strong rPFS and OS benefit**

**Highly selective AKT inhibitor**

- Oral, highly specific inhibitor of all three activated isoforms of AKT, blocking the PI3K/AKT signaling pathway and potentially preventing cancer cell growth and survival
- Clinical development in tumors with high frequency of PI3K/AKT pathway activation (TNBC, HR+ mBC, CRPC)

**Phase II (A.MARTIN):**

- **rPFS (400mg dose)**
  - HR$^*$ = 0.75 (0.54, 1.05)
  - $P$ value = 0.17
  - Median 6.4 mo vs 8.2 mo; HR=0.75; Dose-dependent improvement was observed in OS
  - PTEN loss (which leads to elevated PI3K/Akt pathway activation) was associated with an improved rPFS outcome as measured by NGS, FISH and IHC
  - Ph III (IPATential150) results expected in 2020

**Assays:**

- IHC detection of PTEN protein loss in formalin-fixed, paraffin-embedded tissue
- Strong concordance to DNA technologies (NGS and FISH)

De Bono J.S. et al., ASCO 2016; De Bono J.S. et al., ESMO 2016; mCRPC=metastatic castration resistant prostate cancer; rPFS=radiographic progression free survival; HR=hazard ratio; abi=abiraterone; OS=overall survival; NGS=next generation sequencing; FISH=fluorescence in situ hybridization; IHC=immunohistochemistry
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Pan tumor franchise
First pan tumor approval for NTRK+ solid tumors with CNS disease

**Selective NTRK/ROS1 inhibitor**

- Selective, CNS-active inhibitor of ROS1/NTRK/ALK tyrosine kinases
- Activating ROS1 rearrangements occur in 1-2% of NSCLC
- Activating rearrangements in TRK have been identified in >17 different solid tumors, including head and neck, thyroid, sarcoma and brain

**Phase II (ALKA; STARTRK-1/2):**

- ORR of 57% in NTRK+ solid tumors observed across 10 tumor types; ORR was similar in patients with and without baseline CNS disease
- Rozlytrek has systemic and intracranial efficacy and is a potential treatment option for patients with NTRK+ solid tumors with primary and metastatic CNS disease (high unmet need)

**FMI NGS assay:**

- Detects all classes of genetic alterations in 324 oncogenes + CIT biomarkers MSI and TMB
- 18 therapies currently approved for inclusion in the report

Siena S. et al., XXX; HR=hazard ratio; mOS=median overall survival; mPFS=median progression free survival
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Ovarian cancer: Tecentriq + Avastin in front line OC
Ph III first in class results expected in 2020

Ph III (IMaGYN050) trial design:

- Ph III (PAOLA-1) results for olaparib + Avastin in 1L OC to be presented at ESMO
- Ph III (IMaGYN050) results for all comers and PDL1+ patients expected in 2020
Melanoma: Tecentriq + Zelboraf + Cotellic in 1L BRAF+ mM
ORR of 82% and good durability; Ph III results expected in 2019

Ph I (NCT01656642) results:

<table>
<thead>
<tr>
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<th>T + Z + C (N=38), n (%)</th>
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<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>

- Triplet has a manageable safety profile
- Estimated median duration of response 10.6m and mPFS 12.9m (data immature)
- Triplet may differentiate on durability
- Ph III (IMspire150/TRILOGY) results expected in 2019

Sullivan R. et al, ASCO 2017; mM=metastatic melanoma; ORR=overall response rate; CR=complete response; PR=partial response; SD=stable disease; PD=progressive disease; Cotellic in collaboration with Exelixis; Zelboraf in collaboration with Plexxikon
Liver cancer: Tecentriq + Avastin in 1L HCC
Strong ORR, long durability and high number of CRs observed

Ph Ib (NCT02715531) results Arm A (Tecentriq+Avastin):

<table>
<thead>
<tr>
<th></th>
<th>Arm A: Tecentriq + Avastin</th>
<th>N = 104</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IRF RECIST 1.1</td>
<td>IRF HCC mRECIST</td>
</tr>
<tr>
<td>Confirmed ORR, n (%) (95% CI), %</td>
<td>37 (36) (26 – 46)</td>
<td>41 (39) (30 – 50)</td>
</tr>
<tr>
<td>CR, n (%)</td>
<td>12 (12)</td>
<td>16 (15)</td>
</tr>
<tr>
<td>PR, n (%)</td>
<td>25 (24)</td>
<td>25 (24)</td>
</tr>
<tr>
<td>DCR, n (%)</td>
<td>74 (71)</td>
<td>74 (71)</td>
</tr>
<tr>
<td>On-going response, n (%)</td>
<td>28 (76)</td>
<td>28 (76)</td>
</tr>
<tr>
<td>Median DOR (mo)</td>
<td>NE (11.8 – NE)</td>
<td>NE (11.8 – NE)</td>
</tr>
<tr>
<td>DOR range (mo)</td>
<td>1.6+ – 31.0+</td>
<td>1.6+ – 31.0+</td>
</tr>
<tr>
<td>≥ 9 mo, n (%)</td>
<td>20 (54)</td>
<td>25 (61)</td>
</tr>
<tr>
<td>≥ 12 mo, n (%)</td>
<td>11 (30)</td>
<td>11 (27)</td>
</tr>
</tbody>
</table>

- Confirmed ORR is 36% per IRF-assessed RECIST 1.1 with 12% achieving a complete response; mDOR has not been reached with 76% of responses ongoing per IRF-assessed RECIST 1.1
- Ph I update Arm F (Tecentriq+Avastin vs Tecentriq) to be presented as late breaker at ESMO
- Ph III (IMbrave150) results (Tecentriq+Avastin vs sorafenib) expected in Q4 2019

Lee M.S. et al. APPLE 2019 (Data cutoff: 14 June 2019; median follow-up: 12.4 months); ORR=objective response rate; DOR=duration of response; CR=complete response; PR=partial response; PD=progressive disease; SD=stable disease; DCR=CR+PR+SD; SLD=sum of largest diameters. NE=not evaluable or missing; INV=investigator; IRF=independent review facility

![Best objective response and reduction in target lesion per IRF-assessed RECIST v1.1](image-url)
Our technology platforms in cancer

*Roche pipeline includes differentiated therapeutic platforms*

<table>
<thead>
<tr>
<th><strong>Small molecules</strong></th>
<th><strong>Bi-specifics</strong></th>
<th><strong>Fusion protein</strong></th>
<th><strong>mAb</strong></th>
<th><strong>ADC</strong></th>
<th><strong>Personalized mRNA vaccine</strong></th>
<th><strong>Personalized T cells</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Small molecules" /></td>
<td><img src="image2.png" alt="Bi-specifics" /></td>
<td><img src="image3.png" alt="Fusion protein" /></td>
<td><img src="image4.png" alt="mAb" /></td>
<td><img src="image5.png" alt="ADC" /></td>
<td><img src="image6.png" alt="Personalized mRNA vaccine" /></td>
<td><img src="image7.png" alt="Personalized T cells" /></td>
</tr>
</tbody>
</table>

- **ADC=antibody-drug conjugate; iNeST=Individualized Neoantigen-Specific Therapy**

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- ipatasertib
- idasanutlin
- PI3Kα inhibitor
- SERD

- mosunetuzumab
- CD20 x CD3
- CEA x CD3
- Her2 x CD3
- glypican-3 x CD3

- FAP x IL2v

- aTIGIT (tiragolumab)

- Polivy
- Kadoya

- iNeST

- Patient’s neo-antigens for anti-tumour immune response

- Activated T cell with neoantigen specificity

---

- Target oncogenes, induce apoptosis, suppress tumor growth, etc.
- Engage and activate T cells to kill tumour cells
- Amplify immune response
- Amplify immune response
- Targeted toxic payload
- Patient’s neo-antigens for anti-tumour immune response
- Programmed T cells
CIT evolution

Investing in new technologies

First wave
Checkpoint inhibitors monotherapy & PD-L1 IHC
- Tecentriq (2016)

Second wave
Combine with existing medicines & TMB, MSI, blood based NGS, pan tumor
- Tecentriq + chemo
- Tecentriq + Avastin, Cotellic, Zelboraf, Tarceva, Alecensa, Gazyva, Herceptin, Perjeta, Kadcyla

Third wave
Expand to novel CITs including novel Ab formats & advanced diagnostics
- Immune doublets: Tecentriq + CIT 1, CIT 2…
- Immune doublets: CIT 1 + CIT 2
- e.g. CD20 x CD3; aFAP-IL2v FP; aTIGIT etc.

Fourth wave
Truly personalized CIT & neoantigen sequencing, RNAseq
- Combos/NMEs/"programmed" immune cells targeted at individual immune profiles e.g. iNEST; Adaptive Biotechnologies etc.

= approved
Upcoming conferences in 2019*

**Hematology franchise:**
- mosunetuzumab: Ph I (GO29781) safety/efficacy update in R/R NHL
- CD20 x CD3: Ph I results for various combinations
- Polivy + Gazyva + lenalidomide: Ph I (GO29834; inHarmony) in R/R FL

**Lung franchise:**
- Tecentriq: Ph III (IMpower110): 1L PDL1+ non-sq and sq NSCLC

**Breast franchise:**
- Perjeta + Herceptin: Ph III (APHINITY) 2nd OS 5-year update in eBC

**Tumor agnostic franchise:**
- Rozlytrek: Ph I/ib efficacy update in NTRK1/2/3+ tumors and ROS1+ NSCLC

**GU/GI franchise:**
- Tecentriq + chemo: Ph III (IMvigor130) in 1L mUC
- Tecentriq + Avastin: Ph III (IMbrave150) in 1L HCC
- Tecentriq + Avastin: Ph I (GO30140) Arm F update in 1L HCC

**Immunology franchise:**
- Gazyva + SOC: Ph II (NOBILITY) in lupus nephritis

* Planned submissions (to be confirmed); Outcome studies are event driven, timelines may change
Doing now what patients need next