At the Forefront of R&D Innovation and Breakthrough Treatments

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Executive Summary

• Genentech and Roche are innovation companies
  – **Drill-deep** science delivers breakthrough and transformative medicines
  – **Substantial innovation-focused investment** fuels growth

• Robust portfolio in immunology, ophthalmology, neurodegeneration and infectious diseases

• **Continued oncology leadership**
  – Focus on both **molecular oncology** and **immuno-oncology**
  – Pioneer **novel technology platforms**
Multiple R&D centers drive innovation

Autonomous innovation centers

- **gRED**
- **pRED**
- Chugai

Global Product Development
- Manufacturing
- Commercialization

Diversity, Creativity, Experimentation
- Scale, Reach, Delivery

gRED=Genentech Research and Early Development; pRED=Pharma Research and Early Development
Our drill-deep science creates transformative medicines

Scientific insights

Initial product

Label expansion

New drugs

New therapeutic areas

HER-2 BC biology and ADC technology

B-cell biology

Earlier line breast cancer
Gastric cancer

Earlier line NHL
CLL

Immunology

Multiple Sclerosis
gRED is a publications powerhouse

~380 Publications in 2018
~10 in Cell, Nature and Science

Key Benefits

- Progress science
- Recruit top talent
- Recognition for scientists
- Attract partners to collaborate and expand business opportunities
Our science makes Roche the partner of choice for outside innovation
Our drill-deep strategy delivers breakthrough therapies

25 BTDs in six years
6 in 2018

Oncology
Ophthalmology
Neuroscience
Immunology
Infectious Disease

- Lucentis Diabetic retinopathy
- Alecensa Lung cancer
- Gazyva CLL
- Tecentriq Bladder cancer

- Actemra Systemic Sclerosis
- Hemlibra Hemophilia A with factor VIII inhibitors
- Esbriet IPF
- Venclexta P17 deletion CLL
- Tecentriq Lung cancer

- Actemra Giant cell arthritis
- Rituxan Pemphigus vulgaris
- Alecensa 1L ALK+ NSCLC
- Venclexta + Rituxan R/R CLL
- Venclexta + HMA Acute myeloid leukemia

- Ocrevus Primary progressive MS
- polatuzumab vedotin + BR R/R DLBCL
- Venclexta + LDAC Acute myeloid leukemia
- Zelboraf Erdheim-Chester

- satralizumab NMOSD
- balovaptan Autism
- Xolair Food allergies
- Tecentriq + Avastin 1L hepatocellular carcinoma
- entrectinib NTRK-positive solid tumors
- Hemlibra Hemophilia A without factor VIII inhibitors
- Kadcyla Adjuvant HER2+ BC

- 2013
- 2014
- 2015
- 2016
- 2017
- 2018
- 2019
~70% of Genentech/Roche molecules are first-in-class
Innovation propels Roche through biosimilars impact

New Products as % of Total Pharma Sales

<table>
<thead>
<tr>
<th>Year</th>
<th>Erivedge</th>
<th>Perjeta</th>
<th>Kadcyla</th>
<th>Gazyva</th>
<th>Esbriet</th>
<th>Cotellic</th>
<th>Alecensa</th>
<th>Tecentriq</th>
<th>CHFm</th>
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<tbody>
<tr>
<td>2015</td>
<td>8%</td>
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<tr>
<td>2016</td>
<td>11%</td>
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<tr>
<td>2017</td>
<td>15%</td>
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<tr>
<td>2018</td>
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</table>

Source of Revenue Growth

<table>
<thead>
<tr>
<th>Year</th>
<th>Pharma new products</th>
<th>Pharma other products</th>
<th>Pharma biosimilars exposed</th>
<th>Diagnostics division</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>+3,201</td>
<td>-1,199</td>
<td>+745</td>
<td>-800</td>
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<tr>
<td>2018</td>
<td>53,299</td>
<td>56,846</td>
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</tbody>
</table>

All absolute values are presented in CHFm reported; 1 Erivedge, Perjeta, Kadcyla, Gazyva, Esbriet, Cotellic, Alecensa, Tecentriq, Ocrevus, Hemlibra, and Xofluza; 2 MabThera and Herceptin in Europe and Japan
Record number of NMEs at pivotal stage

<table>
<thead>
<tr>
<th>NMEs</th>
<th>FY 2015</th>
<th>FY 2016</th>
<th>FY 2017</th>
<th>FY 2018</th>
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</thead>
<tbody>
<tr>
<td>Hemlibra</td>
<td>5</td>
<td>5</td>
<td>4</td>
<td>3</td>
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<tr>
<td>idasanutilin</td>
<td>27</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>tасelisib</td>
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<tr>
<td>Venclexta</td>
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<tr>
<td>Alecensa</td>
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<tr>
<td>Tecentriq</td>
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<tr>
<td>lampalizumab</td>
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<tr>
<td>satralizumab</td>
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<tr>
<td>gantenerumab</td>
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<tr>
<td>Ocrevus</td>
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<tr>
<td>lebrikizumab</td>
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<td></td>
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<tr>
<td>etrolizumab</td>
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NME=new molecular entities; FDC=Fixed dose combination; SC=Subcutaneous; PDS=Port delivery system; ASO=Antisense oligonucleotide
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  - Focus on both **molecular oncology** and **immuno-oncology**
  - Pioneer **novel technology platforms**
Half of gRED portfolio is outside of oncology

Early Dev | Phase 1 | Phase 2 | Phase 3 | Registration | Marketed
---|---|---|---|---|---
NME | mosunetuzumab | iNeST (PCV) | ipatasertib | polatuzumab vedotin | Avastin
NME | HER2/CD3 TDB | iNeST (PCV) | etrolizumab | | Cotellic
NME | NME (RG6109) | NME (RG6160) | | | Erivedge
NME | NME (RG6148) | NME (RG6148) | NME (RG6116) | | Herceptin
NME | mPI3K alpha (GDC-0077) | mPI3K alpha (GDC-0077) | | | Kadcyla
NME | SERD (GDC-9545) | Anti-ST2 | | | Perjeta
NME | Belvarafenib | fenebrutinib | | | Tarceva
NME | GDC-0167 | IL22 Fc | | | Tecentriq
NME (RG6151) | | | | | Venclexta
NME (RG6173) | | | | | Rituxan/MabThera
NME (RG6174) | | | | | Pulmozyme
Anti-FGFR1/KLB | | | | | Xolair
NME (RG6147) | | | | | Ocrevus
DLK Inh | | | | | Lucentis
Anti-S. Aureus TAC | | | | | Activase

Refer to Roche 2018 FY results appendix for details
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gRED’s next-generation CIT pipeline targets different recognition and action steps.

**Today’s highlights**

- Individualized neoantigen specific vaccine

**Recognition**

- Priming and activation (APCs & T cells)
- Cancer antigen presentation (dendritic cells/APCs)
- Release of cancer cell antigens (cancer cell death)

**Action**

- Trafficking of T cells to tumors (CTLs)
- Infiltration of T cells into tumors (CTLs, endothelial cells)
- Recognition of cancer cells by T cells (CTLs, cancer cells)
- Killing of cancer cells (Immune and cancer cells)

- mosunetuzumab
- Anti-HER2/CD3
- NMEs
- Anti-PD-L1/Tecentriq
- tiragolumab
Mosunetuzumab engages T-Cells for tumor killing

Full-length humanized IgG1 antibody

Redirects T-cells to engage and eliminate malignant B cells

Off-the-shelf treatment

Mosunetuzumab

CD20
B-cell

CD20
Target +
tumor cell

Immune synapse formation

Processive killing

Granzyme & Perforin

Dead
Tumor cell

Mosunetuzumab

IgG1

CD3
T-cell

T-cell

T-cell activation

Target + tumor cell

CD20

IgG1

CD3

T-cell
Mosunetuzumab shows compelling efficacy and safety

Mosunetuzumab: Ph I/ Ib dose escalation

- **Durable CRs** as a single agent in late-line indolent and aggressive NHL
  - CRs in patients refractory to R-CHOP and to CAR-T
  - No relapses observed to date in R/R FL
- **Safety profile appears tolerable**: most AEs are mild, transient and reversible
- **Ongoing combination trials** with Tecentriq, polatuzumab vedotin and CHOP

**ORR 16/47 (34.0%)**
CR 9/47 (19.1%)

**ORR 18/26 (69.2%)**
CR 10/26 (38.5%)

Budde L., et al, ASH 2018; Hutchings, M., et al, ASH 2018; CR=complete response; SPD=sum of the product diameters; ORR=objective overall response; R/R=relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; tr=transformed; CAR-T=chimeric antigen receptor; CHOP= cyclophosphamide, doxorubicin, vincristine and prednisone
Mosunetuzumab patient shows complete response after CAR-T failure

PET scan

No evidence of disease after 1 year in remission

Relapse following CAR-T therapy

Complete response following 3 cycles of mosunetuzumab

CAR-T=chimeric antigen receptor
Our TDB platform has created a new pipeline

**CD20**
- B-cell malignancies

**NME**
- Multiple Myeloma

**HER2**
- Breast cancer

**Clinical stage**

**Pre-clinical stage**

Various solid and liquid tumors

TDB=T-cell dependent bispecific antibody
Our neoantigen strategy includes vaccine and T cell therapies

Neoantigen targeting is the best approach to harness T cell immunity in cancer

Tumor sample → Mutation identification → Neoantigen prediction

TCR=T-cell receptor; MHC=major histocompatibility complex

mRNA

virus

DNA

Vaccine

Engineered killer T cells

TCR=T-cell receptor; MHC=major histocompatibility complex
Vaccine and T cells are complementary approaches

Recognition

Action

Individualized vaccine (in collaboration with BioNTech)

Phase II

Neo-T (in collaboration with Adaptive)

Preclinical
Leading the way in neoantigen T cell therapies with Adaptive

Identification of Optimal TCRs

Select antigens → Evaluate TCRs

Manufacturing of Cell Therapy Product

T cell engineering → Product QC

TCR=T-cell receptor; QC=quality control
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Patients continue to benefit from gRED innovation

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<th>Phase 2</th>
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<th>Registration</th>
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<td>Cotellic</td>
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Cell colors indicate:
- Blue: Oncology
- Light Blue: Immunology
- Orange: Neuroscience
- Light Purple: Ophthalmology
- Yellow: Metabolism
- Green: Infectious Diseases

Refer to Roche 2018 FY results appendix for details
Doing now what patients need next