At the Forefront of R&D Innovation and Breakthrough Treatments
Michael Varney | Head of Genentech Research and Early Development

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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 Global Innovation

Autonomous innovation centers

- gRED
- pRED
- Chugai

Research
Early Development

Worldwide execution

- Global Product Development
- Manufacturing
- Commercialization

Diversity, Creativity, Experimentation

Scale, Reach, Delivery

gRED=Genentech Research and Early Development; pRED=Pharma Research and Early Development
Premier Innovation Center
Created the world’s largest biotech hub

San Francisco Bay Area

Genentech Research and Early Development

Key Benefits
• Team: 2,200 doing pioneering science
• Innovation: ~20,000 patents granted
• Publication: ~400 publications/year
• Collaborations: >120 globally

Bay Area Life Science Hub*
• Employees: 82,568
• Funding: >$5B VC + > $1B NIH

*California Life Sciences Industry 2018 and 2019 Reports
gRED Is a Publication Powerhouse

~400 Publications in 2019
13 in Cell, Nature and Science

Key Benefits

- Progress science
- Recruit top talent
- Recognition for scientists
- Attract partners to collaborate and expand business opportunities
Innovation Propels Roche Growth

All absolute values are presented in CHFm reported; ¹ Erivedge, Perjeta, Kadcyla, Gazyva, Esbriet, Cotelic, Alecensa, Tecentriq, Ocrevus, Hemlibra, Xofluza, Polivy, and Rozlytrek; ² MabThera and Herceptin in Europe and Japan; ³ Avastin and Herceptin in US Jul-Dec & MabThera/Rituxan in US Nov-Dec
Foundation for gRED Early Drug Development
Building the Pipeline of the Future

Treat * Restore * Cure
Putting the patient first

Science without Borders
Being a Partner of Choice

Human – Machine Partnership
Novel ways of new target discovery

Drug the Undruggable
Focus on increasingly difficult targets

Clear the Path
We Are Creating the Next Wave of Transformative Medicines

<table>
<thead>
<tr>
<th>Oncology</th>
<th>Neuroscience</th>
<th>Ophthalmology</th>
<th>Immunology</th>
<th>Infectious Diseases</th>
<th>Opportunistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunotherapy, Solid Tumors, Hematology</td>
<td>Neuroprotection, Pain</td>
<td>AMD, Geographic Atrophy, Diabetic Retinopathy</td>
<td>Respiratory, Gastrointestinal, Rheumatology, Allergy</td>
<td>ATB-resistant Gram negative bacteria, Microbiome</td>
<td>Nonalcoholic steatohepatitis, Ischemic heart disease</td>
</tr>
</tbody>
</table>

Treat * Restore * Cure
gRED’s **Drill-Deep** Science Creates Transformative Medicines

Scientific insight

Initial product

Label expansion

New drug

New area

**HER-2 BC biology & ADC technology**

- Earlier line breast cancer
- Gastric cancer

**B-cell biology**

- Earlier line NHL
- CLL

**Immunology**

- Immunology

**Multiple Sclerosis**

Roche

10
Roche’s 31 Breakthrough Therapy Designations in 7 years
Reflecting our drill-deep research strategy

- **Luxturna**: RPE-65 mutation-associated retinal dystrophy
- **Lucentis**: Diabetic retinopathy
- **Actemra**: Giant cell arthritis
- **Actemra**: Systemic Sclerosis
- **SPK-9001**: Hemophilia B
- **Alecensa**: Hemophilia A with factor VIII inhibitors
- **Venclexta**: P17 deletion CLL
- **Venclexta + Rituxan**: R/R CLL
- **Venclexta + LDAC**: Acute myeloid leukemia
- **Zelboraf**: Erdheim-Chester
- **Ocrevus**: Primary progressive MS
- **Rituxan**: Pemphigus vulgaris
- **polatuzumab vedotin + BR**: R/R DLBCL
- **entrectinib**: NTRK-positive solid tumors
- **balovaptan**: Autism
- **satralizumab**: NMOSD
- **Xolair**: Food allergies
- **Gazyva**: Lupus nephritis
- **Cotellic**: Histiocytic neoplasms
- **Kadcyla**: Adjuvant HER2+ BC
- **Genentech's 21 Breakthrough Therapy Designations in 7 years Reflecting our drill-deep research strategy**

**2013**
- **Tecentriq**: Lung cancer
- **Gazyva**: CLL
- **Alecensa**: Lung cancer
- **Esbriet**: IPF
- **Luxturna**: RPE-65 mutation-associated retinal dystrophy

**2014**
- **Lucentis**: Diabetic retinopathy
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**2015**
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**2019**
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- **Cotellic**: Histiocytic neoplasms
- **Kadcyla**: Adjuvant HER2+ BC
~70% of Genentech/Roche Molecules Are First-in-Class
Our Science Makes Us the Partner of Choice for Outside Innovation
We Focus On Increasingly Difficult Targets

- Drugged: 1,000 (25%)
- "Undruggable" Hard-to-Drug: 3,000 (75%)
- Disease Modifying: 4,000 (20%)
- Total: ~20,000 genes

We play here

Drug the Undruggable
Platform Diversity Drives Success in Attacking Difficult Targets

- **Macrocycles**: DNA Encoded Library Platform, Quadrillion of Molecules
- **CIDES**: Chemical Inducer of Degradation
- **CKPs**: Cystine Knot Peptides
- **Others Undisclosed**: Top Secret
- **Antibody-Mediated Delivery**: Antibody-Mediated Delivery
- **Tissue Targeting & Tumor Inducible Activation**: Tissue Targeting & Tumor Inducible Activation
- **RNA Disrupters**: RNA Disrupters
- **Biomaterials for LM, SM Delivery**: Immune Tolerance Peptide coated MHC nanoparticles Vaccines

**Drug the Undruggable**
# gRED Utilizes Differentiated Platforms to Benefit Cancer Patients

<table>
<thead>
<tr>
<th>Small molecules</th>
<th>Bi-specifics</th>
<th>Engineered cytokines</th>
<th>mAb</th>
<th>ADC</th>
<th>Personalized mRNA vaccine</th>
<th>Personalized Engineered T cells</th>
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<tbody>
<tr>
<td>ipatasertib</td>
<td>Mosunetuzumab</td>
<td>IL-15(^1)</td>
<td>Tecentriq aTIGIT (tiragolumab)</td>
<td>Polivy Kadcyla</td>
<td>iNeST platform: mRNA-LPX Liposome</td>
<td>Activated T cell with neoantigen specificity</td>
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<tr>
<td>PI3Kα inhibitor SERD</td>
<td>FcRH5 x CD3 HER2 x CD3</td>
<td></td>
<td></td>
<td></td>
<td>mRNA</td>
<td></td>
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<tr>
<td>Target oncogenes, suppress tumor growth</td>
<td>Engage and activate immune cells to kill tumour cells</td>
<td>Amplify immune response</td>
<td></td>
<td>Targeted toxic payload</td>
<td>Patient’s neo-antigens for anti-tumour immune response</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) in collaboration with Xencore; \(^2\) in collaboration with BioNTech; \(^3\) in collaboration with Adaptive Biotechnologies
Selective PI3 Kinase Program
PI3K/AKT is the Most Frequently Mutated Pathway in Cancer

14 million cancer patients diagnosed annually worldwide, ~17% are PIK3CA mutant
2.4M patients

Growth factor receptors

PIK3α

PI3Kβ

PI3Kδ

PI3Kγ

Ras

PIP2

PIP3

PTEN

Thr308

Ser473

PI3K/AKT

Cell cycle, proliferation

Cell survival

Protein synthesis, cell growth

mTORC2

mTORC1

PI3K/AKT signaling pathway:
- Growth factor receptors activate PI3K/AKT
- PIK3CA mutation

Tumor Type | PIK3CA mutation
---|---
Breast
  • HR+ | 40-45%
  • Her2+ | 20-30%
  • TNBC | 8%
Endometrial | 22-31%
Colon | 13-20%
Bladder | 14-20%
Cervix | 11-24%
HNSCC | 11-16%
Gastric | 5-9%
Ovarian CC | 33%
GDC-0077 has Potential to be Best In Class PI3K Inhibitor

Our PI3K alpha inhibitor leverages mutant degrader mechanism of action

Best in-class molecular properties:
- More selective for PI3Kα
- Degradation of mutant PI3Kα
- Greater, more durable target inhibition

Potential for clinical differentiation:
- Increased efficacy
- Greater safety margins
- Combination with CDK4/6i + ET
Phase I Data Differentiates GDC-0077 from Other PI3K Inhibitors

• Well tolerated with improved safety
  – No colitis (58 patients on GDC-0077 > 5 months)
  – Most frequent related adverse event: low grade hyperglycemia
  – Low rate of discontinuation due to adverse event: 1/115 patients

• Anti-tumor activity alone and with endocrine-based therapies
  – Able to combine at its single agent recommended Phase II dose with letrozole and palbociclib at standard doses
GDC-0077 Demonstrates Best in Class Efficacy

- **Single agent activity >> competitors** (GDC-0077 ORR 21% vs alpelisib 4%*)
- GDC-0077 **can safely combine** at its single agent recommended Ph II dose with palbociclib + letrozole at standard approved doses

*Cross trial comparison*
# Robust gRED Portfolio Across Therapeutic Areas

<table>
<thead>
<tr>
<th>Early Dev</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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<tr>
<td>NME</td>
<td>Anti-FcRH5/CD3</td>
<td>iNeST (PCV)</td>
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<td>Avastin</td>
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<td>Anti-ST2</td>
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Doing now what patients need next