Roche Pharma Day 2020

14 September 2020
Roche Pharma Day 2020

Welcome

Karl Mahler | Head of Investor Relations and Roche Group Planning
Agenda

Welcome
Karl Mahler, Head of Investor Relations and Roche Group Planning

Pharma Strategy: Sustainable growth, more patient benefits, and less cost to society
Bill Anderson, CEO Roche Pharmaceuticals

Commercial Opportunities
Teresa Graham, Head Pharma Global Product Strategy (GPS)

Short break

Late Stage Pipeline Oncology & Non-malignant Hematology
Levi Garraway, Chief Medical Officer and Head Global Product Development

Late Stage Pipeline Neuroscience
Paulo Fontoura, Global Head Neuroscience and Rare Diseases Clinical Development

Late Stage Pipeline Immunology & Ophthalmology
Cristin Hubbard, Head I2O (Immunology, Infectious Diseases, Ophthalmology) GPS

Infectious Diseases: A close look at our HBV pipeline
John Young, Global Head of Infectious Diseases, pRED

Late Stage Infectious Diseases: Influenza & SARS-CoV-2
Cristin Hubbard, Head I2O (Immunology, Infectious Diseases, Ophthalmology) GPS

Q&A
36 Breakthrough Therapy Designations received since 2013
Reflecting the quality of our research

<table>
<thead>
<tr>
<th>Year</th>
<th>Molecule</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>2020</td>
<td>mosunetuzumab</td>
<td>3L+ FL</td>
</tr>
<tr>
<td></td>
<td>Tecentriq</td>
<td>unresectable or metastatic ASPS</td>
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<td></td>
<td>Esbriet</td>
<td>uILD</td>
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<tr>
<td>2019</td>
<td>Gavreto</td>
<td>RET fusion-positive NSCLC</td>
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<tr>
<td></td>
<td>Gavreto</td>
<td>RET mutation-positive MTC</td>
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<tr>
<td></td>
<td>Cotellic</td>
<td>Histiocytic neoplasms</td>
</tr>
<tr>
<td></td>
<td>Gazyva</td>
<td>Lupus nephritis</td>
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<tr>
<td></td>
<td>rhPentraxin-2 (PRM-151)</td>
<td>IPF</td>
</tr>
<tr>
<td></td>
<td>Venclexta + Gazyva</td>
<td>1L unfit CLL</td>
</tr>
<tr>
<td></td>
<td>Kadalya</td>
<td>Adjuvant HER2+ BC</td>
</tr>
<tr>
<td>2018</td>
<td>SPK-8011</td>
<td>Hemophilia A</td>
</tr>
<tr>
<td></td>
<td>Enspryng</td>
<td>NMOSD</td>
</tr>
<tr>
<td></td>
<td>Xolair</td>
<td>Food allergies</td>
</tr>
<tr>
<td></td>
<td>Tecentriq + Avastin</td>
<td>1L HCC</td>
</tr>
<tr>
<td></td>
<td>Hemlibra</td>
<td>Hemophilia A non-inhibitors</td>
</tr>
<tr>
<td></td>
<td>Rozlytrek</td>
<td>NTRK+ solid tumors</td>
</tr>
<tr>
<td>2017</td>
<td>Polivy + BR</td>
<td>R/R DLBCL</td>
</tr>
<tr>
<td></td>
<td>Venclexta + LDAC</td>
<td>1L unfit AML</td>
</tr>
<tr>
<td></td>
<td>Zelboraf</td>
<td>BRAF-mutated ECD</td>
</tr>
<tr>
<td></td>
<td>Rituxan</td>
<td>Pemphigus vulgaris</td>
</tr>
</tbody>
</table>
Roche Pharma Day 2020

Pharma Strategy: Sustainable growth, more patient benefits, and less cost to society

Bill Anderson | CEO Roche Pharmaceuticals
Roche has a strong track record of innovation

*Industry leading medicines as basis for our continuous growth*

Sales excluding OTC at 2019 average exchange rates; Approved medicines shown do not represent the entire portfolio rather a selection, timeline reflects year of approval.
Innovation driving portfolio rejuvenation
Increasing share of sales coming from recent launches

All absolute values are presented in CHFm reported
New product growth with strong momentum

Considerable optionality

Biosimilar gap (19-24)

Sensitivity analysis: Assuming conservative planning assumptions of 60-70% erosion from biosimilars

Consensus sales growth (19-24)

Post-HY 2020 consensus survey

- Ocrevus: 3.1 bn
- Tecentriq: 4.1 bn
- Hemlibra: 3.0 bn
- Gazyva: 0.7 bn
- Alecensa: 0.8 bn
- Polivy: 1.1 bn
- Enspryng: 0.4 bn
- Evrysdi: 1.4 bn
- Other in-market 2: (0.3) bn
- Pipeline value 3: 3.4 bn

Total: 17.7 bn

Up-side potential to consensus above are:

- **Oncology** (Gavreto, mosunetuzumab, PI3Kαi, SERD),
- **Ophthalmology** (PDS),
- **Neuroscience** (gantenerumab, prasinezumab, SRP-9001),
- **Immunology** (Gazyva in lupus, rhPentraxin-2, crovalimab, etrolizumab in CD),
- **Infectious diseases** (REGN-COV2, chronic HBV)

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1 Gap value including the total HER2+ franchise change from 2019 to 2024; 2 Xolair, Pulmozyme, CellCept, Activase/TNKase, Actemra, Lucentis, Erivedge, Esbriet, Cotceltic, Xofluza, Rozlytrek; 3 golfitamab, tiragolumab, ipatasertib, faricimab, tominersen
What has changed since our Pharma day a year ago?  
Further increased confidence in delivering growth

<table>
<thead>
<tr>
<th></th>
<th>2018-2023 consensus view¹</th>
<th>2019-2024 consensus view²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gap to fill</td>
<td>9.6 bn</td>
<td>9.6 bn</td>
</tr>
<tr>
<td>New product contribution</td>
<td>16.3 bn</td>
<td>17.7 bn</td>
</tr>
<tr>
<td>+6.7 bn CHF</td>
<td></td>
<td>+8.1 bn CHF</td>
</tr>
</tbody>
</table>

Strong new product contribution and ongoing launches driving growth

¹ Roche Post-HY 2019 consensus survey; ² Roche Post-HY 2020 consensus survey
Strong commercial potential throughout late stage portfolio

+23 late-stage assets with large sales potential

15 blockbusters

10 blockbusters

2018

Ocrevus
MabThera
Herceptin
Avastin
Perjeta

Esbriet
Actemra
Lucentis
Xolair
Activase

Phesgo ✔
Polivy ✔
Xofluza ✔
Evrysdi ✔
Enspryng ✔

2020 consensus

Ocrevus
MabThera
Herceptin
Avastin
Perjeta

Esbriet
Actemra
Lucentis
Xolair
Activase

Gavreto ✔
crovalimab ✔
SERD2 ✔
Pl3Koi2 ✔
tiragolumab ✔
glofitamab ✔
tominersen ✔
gantenerumab ✔
faricimab ✔
mosunetuzumab ✔
pDS w/ ranibizumab ✔
rhPentraxin-2 ✔
Gazyva ✔
etrolizumab ✔

1 Venclexta sales are booked by partner AbbVie; 2 RG6171 (GDC-9545); 3 RG6114 (GDC-0077)
Transformation is a key enabler of our Pharma Vision

**Guiding principles & decentralized execution for maximum impact**

Executive Committee focus on agile: start of major changes to increase flexibility and dynamism

- Lifecycle teams, iSquads, Focused areas in PD
- Corporate functions transform
- International commercial model go live, GPS, pRED
- Product Development 2\textsuperscript{nd} phase

**Guiding principles:**

- From silos, functional and top down focus to small empowered accountable teams
- From internal/organization chart orientation to patient and external focus
- From leadership as command & control to setting a vision, architecting the system, coaching, and catalyzing change
In focus: The VITAL model
Dynamic resource allocation

**Vision:** Align work to our vision and purpose

**Improve Performance:** Lower costs for same output

**Talent Flow:** Move talents to highest priority work

**Accountable to Peers:** Share learnings to enhance decision making

**Lucid to All:** Transparency on results, accountable for continuous improvement
# Increasing our productivity and financial flexibility

<table>
<thead>
<tr>
<th>Pharma Technical</th>
<th>Pharma US</th>
<th>Pharma International</th>
<th>Pharma China</th>
<th>Pharma Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>(HY20 vs. HY16)</td>
<td>(HY20 vs. HY16)</td>
<td>(HY20 vs. HY16)</td>
<td>(HY20 vs. HY16)</td>
<td>(HY20 vs. HY16)</td>
</tr>
<tr>
<td>Sales Volume growth</td>
<td>Sales growth</td>
<td>Sales growth</td>
<td>Sales growth</td>
<td>Late stage portfolio*</td>
</tr>
<tr>
<td>+55%</td>
<td>+34%</td>
<td>+14%</td>
<td>+110%</td>
<td>+26%</td>
</tr>
<tr>
<td>Direct spend +1% and</td>
<td>OPEX +5% and</td>
<td>OPEX +10% and</td>
<td>OPEX +8% and</td>
<td>PD spend +23% and</td>
</tr>
<tr>
<td>headcount -19%</td>
<td>headcount -19%</td>
<td>headcount -3%</td>
<td>headcount +25%</td>
<td>headcount +14%</td>
</tr>
</tbody>
</table>

**Maturity of transformation efforts**

* Project count growth
Strong profitability development despite challenging environment

% of sales

46.2% 45.1% 47.2% 47.5% 47.2%

Sales

All absolute values are presented in CHFm reported
Our Pharma Vision 2030
Providing more patient benefit at less cost to society

1. Doubling of medical advances
   - Re-allocation of resources into R&D, while working on and protecting profitability
   - R&D Mission Support

2. Significantly progress other patient benefits
   - Integrated solutions and new engagement models
   - Improved outcomes via enhanced disease management

3. Less cost to society
   - Breakthrough science and insights to reduce cost of disease
   - Reducing societal costs beyond the cost of therapy

Transformation as a key enabler

1 First approval of a new molecule in a new indication
Our Pharma Vision 2030

Providing more patient benefit at less cost to society

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Transformation as a key enabler

\(^1\) First approval of a new molecule in a new indication
Invest in innovation: Assets in Ph III & registration
Strong momentum in the second half 2020

NMEs

<table>
<thead>
<tr>
<th></th>
<th>HY 2016</th>
<th>HY 2017</th>
<th>HY 2018</th>
<th>HY 2019</th>
<th>HY 2020</th>
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<tr>
<td>NME</td>
<td>11</td>
<td>11</td>
<td>9</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>AI</td>
<td></td>
<td></td>
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</tr>
<tr>
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<td>1</td>
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<td>1</td>
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<td>1</td>
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<tr>
<td></td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

**Outlook FY 2020**

23

+10 NMEs to be added until year end

- Gavreto in RET+ NSCLC & thyroid cancer
- SERD Ph III in 1L HR+ mBC
- glofitamab Ph III in r/r DLBCL
- mosunetuzumab Ph III in r/r FL
- crovalimab Ph III in PNH
- REGN-COV2 Ph III in COVID-19 (run by Regeneron)
- rhPentraxin-2 Ph III in IPF
- Gazyva Ph III in Lupus nephritis
- fenebrutinib Ph III in RMS & PPMS
- SRP-9001 Ph III in DMD (run by Sarepta)

NME=new molecular entity; AI=additional indication
Strategic re-allocation of resources

Pharma cost structure

- Cost of sales
- M&D
- G&A
- R&D

Principles for resource allocation

- Re-allocate resources into R&D while working on and protecting profitability
- Optimizing costs and efforts by
  - More targeted and often virtual stakeholder engagement
  - Personalized, digital content & services
- Improve performance by dynamic resource allocation (VITAL model)
Recent deals and partnerships\textsuperscript{1}

\textit{Accelerate drug discovery and driving personalized healthcare}

<table>
<thead>
<tr>
<th>Early stage assets</th>
<th>Late stage assets</th>
<th>Research technologies</th>
<th>Digital &amp; PHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textbf{Dicerna} \textsuperscript{(HBV)}</td>
<td>\textbf{IONIS} \textsuperscript{(tominersen)}\textsuperscript{2}</td>
<td>\textbf{Promedior} \textsuperscript{(rhPentraxin-2)}</td>
<td>\textbf{FOUNDATION MEDICINE} \textsuperscript{(molecular information)}</td>
</tr>
<tr>
<td>\textbf{Secure} \textsuperscript{(NLRP3 inhibitors)}</td>
<td>\textbf{SAREPTA} \textsuperscript{(SRP-9001/DMD)}</td>
<td>\textbf{Spark} \textsuperscript{(gene therapy; SPK-8011)}</td>
<td>\textbf{FRED HUTCH} \textsuperscript{(digital remote monitoring system)}</td>
</tr>
<tr>
<td>\textbf{Adaptive Therapeutics} \textsuperscript{(T-cell therapies)}</td>
<td>\textbf{PTC Therapeutics} \textsuperscript{(risdiplam)}\textsuperscript{2}</td>
<td>\textbf{REGENERON} \textsuperscript{(REGN-COV2)}</td>
<td>\textbf{flatiron} \textsuperscript{(electronic health records)}</td>
</tr>
<tr>
<td>\textbf{4DMT} \textsuperscript{(choroideremia)}</td>
<td>\textbf{blueprint medicine} \textsuperscript{(Gavreto)}</td>
<td>\textbf{VIVIDION} \textsuperscript{(E3 ligases)}</td>
<td></td>
</tr>
</tbody>
</table>

78 new agreements in 2019 focused on

High disease burden / Promising targets / Novel enabling technologies

\textsuperscript{1} Non-exhaustive overview; \textsuperscript{2} at the time of licensing
Our Pharma Vision 2030

Providing more patient benefit at less cost to society

More patient benefit

1. Doubling of medical advances
   - Re-allocation of resources into R&D, while working on and protecting profitability
   - R&D Mission Support

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Transformation as a key enabler

1 First approval of a new molecule in a new indication
# Go-to-market Model

*Strategic shifts until 2030*

<table>
<thead>
<tr>
<th>From</th>
<th>To</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Engagement</strong></td>
<td>&quot;Mass field&quot; largely in-person</td>
</tr>
<tr>
<td></td>
<td>More targeted and often virtual</td>
</tr>
<tr>
<td><strong>Content</strong></td>
<td>Static information</td>
</tr>
<tr>
<td></td>
<td>Personalized, digital content and services</td>
</tr>
<tr>
<td><strong>Content release</strong></td>
<td>Synchronized with field force cycles</td>
</tr>
<tr>
<td></td>
<td>Continuous and real-time</td>
</tr>
<tr>
<td><strong>Customer targeting</strong></td>
<td>Decided by sales representatives</td>
</tr>
<tr>
<td></td>
<td>Supported by advanced analytics</td>
</tr>
<tr>
<td><strong>Conference</strong></td>
<td>Physical attendance</td>
</tr>
<tr>
<td></td>
<td>Virtual and real-time exchange</td>
</tr>
</tbody>
</table>
Evolving customer engagement models: US
Early progress in ”Pioneer” go-first areas

First large pharmaceutical company in US market to develop Eco-system approach

Old structure

New structure

- Empower local decision making
- Providing integrated solutions
Delivering Integrated Solutions

*Using data & insights to improve patient outcomes*

Access to comprehensive genomic profiling (CGP)
- early, personalized diagnosis

Molecular tumor board (MTB) / clinical decision support (CDS)
- personalized care plan

Access to molecularly guided treatment options
- rapid therapy access and innovative access models

Capturing clinical outcomes
- Leveraging RWD for regulatory filings, publications, policy change, innovative access models

More patients on optimal therapy and creation of ‘learning healthcare system’

PHC=personalized healthcare; RWD=real world data
Our Pharma Vision 2030

*Providing more patient benefit at less cost to society*

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### More patient benefit

1. **Doubling of medical advances**
   - Re-allocation of resources into R&D, while working on and protecting profitability
   - R&D Mission Support

2. **Significantly progress other patient benefits**
   - Integrated solutions and new engagement models
   - Improved outcomes via enhanced disease management

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### Less cost to society

3. **I.e.: Earlier, more targeted, efficacious & shorter interventions**
   - Breakthrough science and insights to reduce cost of disease
   - Reducing societal costs beyond the cost of therapy

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1 First approval of a new molecule in a new indication

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Transformation as a key enabler
Responsible pricing strategy: Impact of medicines is at the core, while considering WHO’s fair pricing dimensions

HEALTH IMPACT

Positive impact of medicine for patients, healthcare systems and society.

FUTURE INNOVATION

Pricing strategy allows to invest into high risk and complex disease areas.

Meeting the needs of patients of tomorrow.

SYSTEM CONTEXT

Pricing reflects different healthcare systems & regulatory environments.

Make medicines as affordable as possible.

Innovation available for patients today and tomorrow
Recent examples of responsible pricing

- OCREVUS®: ~25% discount to Rebif list price in the US
- HEMLIBRA: ~50% discount to BPA prophylaxis in the US
- ROZLYTREK®: ~50% discount to Vitrakvi list price in the US

Net price increases in line with medical inflation in the US

- US net price increase below inflation for all medical care expenditures
- US net price increase above inflation for all medical care expenditures

<table>
<thead>
<tr>
<th>Year</th>
<th>US net price increase</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>~25% below inflation</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>~50% below inflation</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>~50% below inflation</td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td>~50% below inflation</td>
<td></td>
</tr>
<tr>
<td>2020*</td>
<td>~50% below inflation</td>
<td></td>
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</tbody>
</table>

Price ceiling for Evrysdi

- Infants: USD < 100K / year
- Maximum Price: USD 340K / year

- ~25% discount to Spinraza in the US

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1 Genentech’s annual average net price increase in the U.S., weighted by sales; 2 for inflation CPI-U Medical Care is used for all medical care expenditures (incl. prescription and non-prescription drugs, medical supplies, physicians’ services, hospital services, and health insurance) – source: U.S. Bureau of Labor Statistics (US BLS); 3 discount at launch; 4 discount over 5-yrs (at max Evrysdi price); 5 average infant weight from the FIREFISH trial; * TTM for CPI-U Medical Care in 2020
Costs to society
Reducing societal costs of disease beyond the cost of therapy

Actemra in COVID-19: Positive trend in time to hospital discharge

Time to hospital discharge/ready for discharge to day 28†

- Median Time to Response: TCZ=20.0 [17.0 to 27.0]; PBO=28.0 [20.0 to NE]
- Potential for freeing up hospital capacity if confirmed in additional studies

Venclexta + Gazyva in CLL: Potential for shorter/curative treatment

Ph III (CLL14) results*

- 90% of MRD-negative patients remained in remission 2 years after treatment
- Fixed treatment duration avoids long term side effects of chronic therapy & generates savings to HC system

Ocrevus in MS: Delaying the need for walking aid

Disability progression in patients with RMS

- Irreversible disability†
- Decreased employment‡
- Consequences of reaching EDSS score ≥6.0 walking aid required
- Expanding the time patients can live independently & continue working

¹ Rosas, et al., 2020, doi: https://doi.org/10.1101/2020.08.27.20183442; ² Fischer, et al., ASH 2019; ³ Tomassini V, et al., MSJ 2019;25:1306–1315; ⁴ Kobelt G, et al., MSJ 2017;23:1123–1136; ICU=intensive care unit; CLL=Chronic lymphoid leukemia; MRD=minimal residual disease; HC=healthcare; RMS=relapsing multiple sclerosis; EDSS=Expanded Disability Status Scale; Venclexta in collaboration with AbbVie
## Strong short- and mid-term news flow

**Diversifying the late stage pipeline and setting new standards of care**

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication</th>
<th>Filing</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>tominersen</td>
<td>Huntington’s</td>
<td>latest 2022</td>
<td>~83k</td>
</tr>
<tr>
<td>gantenerumab</td>
<td>Alzheimer’s</td>
<td>2022</td>
<td>~9,300k (prodromal) ~3,600k (mild)</td>
</tr>
<tr>
<td>SRP-9001</td>
<td>DMD</td>
<td>latest 2023</td>
<td>~21k</td>
</tr>
<tr>
<td>etrolizumab</td>
<td>Crohn’s</td>
<td>2022</td>
<td>~570k (moderate/severe)</td>
</tr>
<tr>
<td>PDS</td>
<td>nAMD DME</td>
<td>2020 2022</td>
<td>nAMD ~3,600k DME ~4,700k</td>
</tr>
<tr>
<td>faricimab</td>
<td>DME nAMD</td>
<td>2021</td>
<td></td>
</tr>
<tr>
<td>Actemra + remdesivir</td>
<td>COVID-19</td>
<td>2021</td>
<td>n/a</td>
</tr>
<tr>
<td>REGN-COV2</td>
<td>COVID-19</td>
<td>2021</td>
<td>n/a</td>
</tr>
<tr>
<td>crovalimab</td>
<td>PNH</td>
<td>2022</td>
<td>~14k</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication</th>
<th>Filing</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gavreto</strong></td>
<td>RET+ NSCLC</td>
<td>filed</td>
<td>~2k (Dx+)</td>
</tr>
<tr>
<td></td>
<td>thyroid cancer</td>
<td></td>
<td>~6k (Dx+)</td>
</tr>
<tr>
<td>Tecentriq</td>
<td>NeoAdj TNBC</td>
<td>2020</td>
<td>~23k</td>
</tr>
<tr>
<td></td>
<td>Adj SCCHN</td>
<td>2021</td>
<td>~8k</td>
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<tr>
<td></td>
<td>Adj RCC</td>
<td>2021</td>
<td>~20k</td>
</tr>
<tr>
<td></td>
<td>(Neo)Adj NSCLC</td>
<td>2021/22</td>
<td>~100k</td>
</tr>
<tr>
<td></td>
<td>Adj HCC</td>
<td>2022</td>
<td>tbd</td>
</tr>
<tr>
<td>Tecentriq + P+H</td>
<td>NeoAdj HER2+ BC</td>
<td>2021</td>
<td>~40k</td>
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<td>ipatasertib</td>
<td>1L/2L TNBC</td>
<td>2020</td>
<td>~11k (Dx+)</td>
</tr>
<tr>
<td></td>
<td>1L mCRPC</td>
<td>2020</td>
<td>~100 (Dx+)</td>
</tr>
<tr>
<td>Polivy</td>
<td>1L DLBCL</td>
<td>2021</td>
<td>~51k</td>
</tr>
<tr>
<td>tiragolumab + T</td>
<td>1L SCLC</td>
<td>2022</td>
<td>~57k</td>
</tr>
<tr>
<td>mosunetuzumab</td>
<td>R/R FL</td>
<td>2021</td>
<td>~3k</td>
</tr>
<tr>
<td>glofitamab</td>
<td>R/R DLBCL</td>
<td>2022</td>
<td>~24k</td>
</tr>
<tr>
<td>Venclexta</td>
<td>R/R MM t(11;14)</td>
<td>2022</td>
<td>~6k (Dx+)</td>
</tr>
<tr>
<td>SERD (RG6171)</td>
<td>2L/3L mBC</td>
<td>2022</td>
<td>~74k</td>
</tr>
</tbody>
</table>

Source: Roche/Genentech, incidence/prevalence in the major markets (US, FR, DE, IT, ES, GB); DMD=duchenne muscular dystrophy; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; NSCLC=non-small cell lung cancer; TNBC=triple-negative breast cancer; SCCHN=squamous cell carcinoma of the head and neck; RCC=renal cell carcinoma; HCC=hepatocellular carcinoma; mCRPC=metastatic castration resistant prostate cancer; DLBCL=diffuse large B-cell lymphoma; SCLC=small cell lung cancer; FL=follicular lymphoma; PNH=paroxysmal nocturnal hemoglobinuria
Replace and extend the business: Improve on the standard of care
Most significant pipeline advances in a year ever

### Replace/extend existing businesses

<table>
<thead>
<tr>
<th>MabThera/Rituxan</th>
<th>Gazyva, Venclexta, Polivy, mosunetuzumab, glofitamab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herceptin</td>
<td>Perjeta, Kadcyla, Phesgo</td>
</tr>
<tr>
<td>Avastin</td>
<td>Tecentriq, Alecensa, Rozlytker, tiragolumab</td>
</tr>
<tr>
<td>Lucentis</td>
<td>Port delivery system (PDS) faricimab</td>
</tr>
<tr>
<td>Tamiflu</td>
<td>Xofluza</td>
</tr>
</tbody>
</table>

### Entering new franchises

- **Oncology:**
  - Tecentriq (mUC, TNBC, SCLC, HCC, mM), ipatasertib (mCRPC), SERD (HR+ BC)
  - Gazyva, Venclexta, Polivy, mosunetuzumab, glofitamab
  - Pi3Kα (RG6114)
  - SERD (RG6171)
  - PI(3)Kαi (RG6114)
  - HR+ mBC (INAVO120)
  - SERD (RG6171)
  - glofitamab
  - mosunetuzumab
  - Venclexta
  - crovalimab

- **Hemophilia A:** Hembira

- **Neuroscience:**
  - Ocrevus (RMS, PPMS)
  - Enspryng (NMOSD)
  - Evrysdi (SMA)
  - tominersen (Huntington)
  - gantenerumab (AD)
  - SRP-9001 (DMD)

- **Immunology:**
  - etrolizumab (CD), Gazyva (Lupus nephritis)

- **Infectious diseases:** REGN-COV2 (COVID-19)

- **PDS**
  - Faricimab (PDS)

### New pivotal trial starts in 2020

- tiragolumab: mNSCLC (SKYSCRAPER-01)
  - ES-SCLC (SKYSCRAPER-02)
  - stage III unresectable NSCLC (SKYSCRAPER-03)
  - locally adv. esophageal cancer (SKYSCRAPER-07/08)
- PI3Kα (RG6114)
- SERD (RG6171)
- glofitamab: 2L+ FL
- mosunetuzumab: 2L+ FL
- Venclexta: 1L fit AML, 1L fit CLL
- crovalimab: PNH (COMMODORE 1/2)
- REGN-COV2: COVID-19 treatment/prophylaxis
- Gazyva: Lupus nephritis (REGENCY)
- rhPentaxin-2: Idiopathic pulmonary fibrosis
- SRP-9001: Duchenne muscular dystrophy
- fenebrutinib: RMS (FENhance 1/2), PPMS (FENtrepid)
- Ocrevus higher dose: RMS (MUSETTE), PPMS (GAVOTTE)
- Diabetic retinopathy without CI-DME (PAVILION)

---

mUC=metastatic urothelial carcinoma; TNBC=triple negative breast cancer; SCLC=small cell lung cancer; HCC=hepatocellular carcinoma; mM=metastatic melanoma; mCRPC=metastatic castration resistant prostate cancer; BC=breast cancer; RMS=relapsing multiple sclerosis; PPMS=primary progressive MS; NMOSD=neuromyelitis optica spectrum disorder; SMA=spinal muscular atrophy; AD=Alzheimer’s disease; DMD=duchenne muscular dystrophy; CD=Crohn’s disease; NSCLC=non-small cell lung cancer; ES-SCLC=extensive-stage small cell lung cancer; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; AML=acute myeloid leukemia; CLL=chronic lymphocytic leukemia; MDS=myelodysplastic syndromes; PNH=paroxysmal nocturnal hemoglobinuria; CI-DME=center-involved diabetic macular edema
Late stage pipeline update

1. Hematology franchise
   - DLBCL: Polivy, gloatimab, mosunetuzumab
   - FL: mosunetuzumab, gloatimab, Polivy
   - AML: Venclexta
   - MM: Venclexta
   - MDS: Venclexta

2. Breast Cancer franchise
   - TNBC: Tecentriq, ipatasertib
   - HR+: SERD (RG6171, PI3Kαi (RG6114)
   - HER2+: Tecentriq

3. Lung Cancer franchise
   - NSCLC: Tecentriq, tiragolumab
   - SCLC: Tecentriq, tiragolumab
   - ALK+: Alecensa
   - ROS1+/NTRK+: Rozlytrek
   - RET+: Gavreto
   - KRAS G12C+: GDC-6063

4. Other oncology
   - CRPC: ipatasertib
   - Thyroid cancer: Gavreto
   - Esophageal cancer: tiragolumab
   - Melanoma: Tecentriq, Cotellic, Zelboraf

5. Non-malignant hematology
   - Hemophilia A: Hemlibra
   - Hemophilia A: Factor VIII Gene Therapy
   - PNH: crovalimab

6. Neuroscience
   - MS: Ocrevus; fenebrutinib
   - SMA: Evrysdi
   - NMOSD: Enspryng
   - AD: gantenerumab, anti-Tau, brain shuttle
   - Huntington’s disease: tominersen
   - DMD: Micro-dystrophin Gene Therapy
   - Parkinson’s disease: prasinezumab

7. Immunology
   - IPF: rhPentraxin-2, Esbriet
   - Myelofibrosis: rhPentraxin-2
   - Lupus nephritis: Gazyva
   - Crohn’s disease: etrolizumab

8. Ophthalmology
   - nAMD, DME, DR: Port Delivery System
   - nAMD, DME, RVO: faricimab

9. Infectious diseases
   - HBV: TLR7 agonist, CpAM, RG6346, RG6084
   - Influenza A/B: Xofluza
   - SARS-CoV2: Actemra
   - SARS-CoV2: REGN-COV2

* For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 20 results presentation appendix or visit the IR homepage.
2020: Positive outlook re-iterated

NME launches
Ocrevus, Perjeta, Hemlibra, Tecentriq, Venclexta, Gazyva, Alecensa, Xofluza, Polivy, Rozlytrek, Phesgo, Evrysdi, Enspryn, Gavreto, mosunetuzumab, glofitamab, ipatasertib, PI3Kαi, SERD, tiragolumab, faricimab, PDS, tominersen, gantenerumab, prasinezumab, SRP-9001, SPK-8011, rhPentraxin-2, crovalimab, etc.
Roche Pharma Day 2020

Commercial Opportunities

Teresa Graham | Head of Global Product Strategy
Supporting patient access during COVID-19

Expanding patient options to support continuity of care

OCREVUS Home Infusion
Launched in Australia

Home use filing accepted by FDA Aug 2020

At home liquid biopsy project initiated in Italy

Patients are self-isolating to minimise their risk of becoming infected with COVID-19

Ocrevus home infusion in partnership with View Health; Foundation Medicine Liquid biopsy in partnership with Egg s.r.l.
1. **Hematology franchise**
   - DLBCL: Polivy, glofitamab, mosunetuzumab
   - FL: mosunetuzumab, glofitamab, Polivy
   - AML: Venclexta
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10. **Oncology / Hematology**
11. **Neuroscience**
12. **Ophthalmology**
13. **Immunology**
14. **Oncology / Hematology**
15. **Immunology**
16. **Oncology / Hematology**
17. **Immunology**
18. **Infectious diseases**
19. **Oncology / Hematology**
20. **Immunology**
21. **Oncology / Hematology**

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Tecentriq
Annualized sales >2b with significant growth opportunities ahead

**1L combinations**
1L SCLC, 1L TNBC, and 1L NSCLC continuing to drive growth ex-US; Launch of HCC next major growth driver with contributions from 1L mUC and BRAF+ Melanoma

**Neoadjuvant / adjuvant**
Continued readouts in early disease: TNBC, NSCLC, SCCHN, RCC, HCC, HER2+ BC

**CIT combinations**
Tecentriq + Tiragolumab has the potential to reset the standard of care in markets where PD-1/PD-L1 already established
Tecentriq + Avastin: A new standard in HCC treatment
First new therapy with survival benefit in HCC in over a decade

HCC is the fourth most common cancer in China

Incidence Rate of Top 10 Cancers in China

Lung
Breast
Stomach
Liver
Colorectum
Esophagus
Cervix
Thyroid
Uterus
Prostate

>750k people / year diagnosed with HCC globally

Tecentriq + Avastin approved in 25 countries. Approval in China and EU expected early Q4

All major global guidelines recommend T+A as a new SOC in HCC

Ongoing development in earlier lines and new combinations

<table>
<thead>
<tr>
<th></th>
<th>Adjuvant</th>
<th>Intermediate</th>
<th>Unresectable</th>
<th>TML</th>
<th>New pipeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>T+A</td>
<td>T+A</td>
<td>T+A</td>
<td>T+A</td>
<td>T+A</td>
<td>T+A+X</td>
</tr>
</tbody>
</table>

T+A = Tecentriq + Avastin; HCC = Hepatocellular Carcinoma; TML = tumor mutational load
## Tecentriq in early disease

**Curative potential for the largest number of patients**

<table>
<thead>
<tr>
<th>Breast</th>
<th>Positive data in neoadjuvant TNBC will be shared with health authorities</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• &gt;50% of TNBC pts treated in neoadjuvant setting</td>
</tr>
<tr>
<td></td>
<td>• Ongoing trials for Tecentriq in adjuvant TNBC and neoadjuvant HER2+ BC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lung</th>
<th>Interim Ph III results for neoadjuvant and adjuvant NSCLC expected 2020/2021</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• 25-35% of NSCLC patients have resectable disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GI/GU</th>
<th>Trials initiated in NMIBC, adjuvant RCC, and adjuvant HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• &gt;2.5x more patients with early UC than metastatic UC</td>
</tr>
</tbody>
</table>

Source: Roche US/EU5 epidemiology; TNBC=triple negative breast cancer; NSCLC=non-small cell lung cancer; NMIBC=non-muscle invasive bladder cancer; RCC=renal cell carcinoma
Tiragolumab (anti-TIGIT) development program

First program with randomized data showing benefit on top of PD-L1

6 randomized trials of tiragolumab + Tecentriq initiated

<table>
<thead>
<tr>
<th>Trial</th>
<th>Indication</th>
<th>Market size</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKYSCRAPER-01</td>
<td>1L NSCLC: PD-L1 high</td>
<td><img src="500m" alt="Symbol" /> <img src="500m-1b" alt="Symbol" /> <img src="%3E1b" alt="Symbol" /></td>
</tr>
<tr>
<td>SKYSCRAPER-02</td>
<td>ES-SCLC</td>
<td><img src="%3E1b" alt="Symbol" /></td>
</tr>
<tr>
<td>SKYSCRAPER-03</td>
<td>Stage III unresectable NSCLC</td>
<td><img src="%3E1b" alt="Symbol" /></td>
</tr>
<tr>
<td>SKYSCRAPER-04</td>
<td>PD-L1+ Cervical Cancer</td>
<td><img src="500m" alt="Symbol" /> <img src="500m-1b" alt="Symbol" /></td>
</tr>
<tr>
<td>SKYSCRAPER-07</td>
<td>Locally advanced ESCC</td>
<td><img src="500m" alt="Symbol" /> <img src="500m-1b" alt="Symbol" /></td>
</tr>
<tr>
<td>SKYSCRAPER-08</td>
<td>China 1L ESCC</td>
<td><img src="500m" alt="Symbol" /> <img src="500m-1b" alt="Symbol" /></td>
</tr>
</tbody>
</table>

Development strategy

1. Build on Tecentriq
2. Expand into early disease
3. Compete in new indications

Additional trials ongoing in HCC, mUC, PDAC, and hematology (MM, NHL)

NSCLC=Non-Small Cell Lung Cancer; ES-SCLC=extensive stage small cell lung cancer; ESCC=esophageal squamous cell carcinoma; HCC=hepatocellular carcinoma; mUC=metastatic urothelial carcinoma; PDAC=Pancreatic ductal adenocarcinoma; MM=multiple myeloma; NHL=non-hodgkins lymphoma
Solid business case for oncogenic driver mutations

High ORR and durable benefit drives long duration of therapy
- Alecensa PFS ~35m in 1L NSCLC vs. ~8m for PD-1/PD-L1; opportunity in early disease

NGS testing rate increasing with new technologies and therapeutics
- FMI liquid biopsy approved (30% of NSCLC patients with insufficient tissue for testing)

Lean and innovative trial design supported by Real World Data
- Comparative RWD for Rozlytrek submitted in US, Europe, Japan, and Canada
- B-FAST study with multiple driver mutation cohorts

Pan-tumor potential across multiple programs
- TAPISTRY: tumor agnostic basket trial across multiple driver mutations and CIT

Rare mutations (≤2%) add up to ~10% of the lung cancer market: ~4bn

Source: Roche; NSCLC=Non-Small Cell Lung Cancer; NGS=next generation sequencing
Alecensa annualized sales >1b with further growth catalysts

Market leader with >70% market share in US, EU, Japan

China driving further growth in international markets
- Significant volume uptake in 2020, following NRDL reimbursement

Expanding into early disease
- ALINA trial in ALK+ adjuvant NSCLC has potential to address 25-35% of ALK+ NSCLC patients

Expanding testing to more patients
- B-FAST trial: Alecensa data in ALK+ patients tested by FMI liquid biopsy presented at ESMO

Tumor agnostic development
- Alecensa arm added to TAPISTRY basket trial: ALK fusion prevalence <1% (excluding NSCLC)

Source: Roche; NSCLC=Non-Small Cell Lung Cancer; NRDL=National Reimbursement Drug List; FMI=Foundation Medicine Inc.
Phesgo US approval
Approved by FDA in June, filed in EU

Administration and observation time reduced from 2.5-7.5 hours to 20-38 minutes

<table>
<thead>
<tr>
<th>Treatment option</th>
<th>Administration and observation schedule*</th>
<th>Total time</th>
</tr>
</thead>
<tbody>
<tr>
<td>H IV P IV</td>
<td>0.5 – 1.5 hours 2 – 6 h 1h 1h</td>
<td>~2.5–7.5 hours</td>
</tr>
<tr>
<td>H SC P IV</td>
<td>2 – 5 min 2 – 6 h 1h 1h</td>
<td>~2–6 hours</td>
</tr>
<tr>
<td>PHESGO</td>
<td>5 – 8 min 15 – 30 min</td>
<td>~20–38 min</td>
</tr>
</tbody>
</table>

Ranges driven by differences in loading and maintenance dose

IV=intravenous; *Ranges driven by differences in loading and maintenance dose; Phesgo in collaboration with Halozyme
High unmet need remains across HR+/HER2- BC
Large addressable population for SERD and PI3K programs

HR+/HER2- BC

40% of HR+ patients have PI3K mutation

Roche molecules targeting both early and metastatic disease

<table>
<thead>
<tr>
<th>eBC</th>
<th>1L mBC</th>
<th>2L/3L mBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ET +/- CDK4/6i</td>
<td>ET + CDK4/6i</td>
<td>ET monotherapy</td>
</tr>
</tbody>
</table>

**Endocrine Therapy**
Given until resistance or visceral disease present

**SERD (RG6171)**
Replace ET as standard of care in all settings

**PI3Kαi (RG6114)**
Combine with SOC In Pi3Km patients

30% of patients become resistant to standard of care

ET=endocrine therapy; HR+ BC=hormone receptor positive breast cancer; TNBC=triple negative breast cancer; eBC=early breast cancer; mBC=metastatic breast cancer;

1 GDC-9545; 2 GDC-0077
Polivy readout in 1L DLBCL in 2021

Opportunity to establish Polivy as standard of care in curative setting

Rapid uptake in R/R DLBCL

- **Strong efficacy**: only agent in R/R DLBCL with OS benefit
- **Well tolerated**: combines with standard of care (BR); no unique safety monitoring requirements
- **Off the shelf**: readily available; administered in any oncology facility, with no hospitalization required

**POLARIX** is the only Ph III trial in 1L DLBCL (non-biomarker)

<table>
<thead>
<tr>
<th>1L</th>
<th>2L</th>
<th>3L+</th>
</tr>
</thead>
<tbody>
<tr>
<td>~50.6k</td>
<td>~15.6k</td>
<td>~9.1k</td>
</tr>
</tbody>
</table>

1L DLBCL treated population is >3x the size of 2L

<table>
<thead>
<tr>
<th>Polivy+R/G-CHP (Ph Ib/II)</th>
<th>R-CHOP (GOYA trial)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>89%</td>
</tr>
<tr>
<td>CR</td>
<td>76%</td>
</tr>
</tbody>
</table>

Ph Ib/II data in 1L DLBCL compares favorably to historical controls despite older population and sicker patients

Source: Roche/Genentech; Polivy in collaboration with Seattle Genetics; DLBCL=diffuse large B-cell lymphoma; BR = Rituxan + Bendamustine
Mosunetuzumab and glofitamab (CD20xCD3)
Potential first in class bispecifics in DLBCL and FL

<table>
<thead>
<tr>
<th>Indication</th>
<th>Unmet Need</th>
<th>Lead Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>R/R FL</td>
<td>Reduction of chemo and quality of life are important for patients</td>
<td>Mosunetuzumab BTD in 3L+ FL; Ph III safety run-in initiated in 2L+ FL</td>
</tr>
<tr>
<td>R/R DLBCL</td>
<td>Highly aggressive disease: patient need for durable efficacy</td>
<td>Glofitamab Glofitamab Ph III safety run-in initiated in combination with GemOx</td>
</tr>
<tr>
<td>1L DLBCL</td>
<td>High efficacy bar established; need therapy which is combinable</td>
<td>Chemo free regimens being explored in Ph Ib for both glofitamab and mosunetuzumab including combinations with Polivy, Gazyva, Tecentriq</td>
</tr>
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Furthest advanced bispecific portfolio with >1000 patients dosed and randomized trials being initiated
Venclexta
Annualized sales >1bn driven by CLL and AML

Developing in indications with >$40B market size by 2025

- **1L CLL**
  - Fixed duration, chemo free regimen, with high MRD-negative responses

- **1L AML**
  - First new medicine in AML in 20 years; >40% US market share in 1L unfit patients

- **Multiple Myeloma**
  - Ph III CANOVA trial underway in ~20% of patients with t11:14 translocation

- **MDS**
  - Encouraging early data in high unmet need population

Market size: Evaluate Pharma estimated market size 2025; 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; Venclexta in collaboration with AbbVie
Hemlibra is a transformational advance for Hemophilia A patients
Continued increase in patients with zero bleeds to >85% after 72 weeks

Source: Treated patients, Hemlibra Epidemiology models 2018 PWHA=People with Hemophilia A
1. **Hematology franchise**
   - DLBCL: Polivy, glositamab, mosunetuzamab
   - FL: mosunetuzamab, glositamab, Polivy
   - AML: Venclexta
   - MM: Venclexta
   - MDS: Venclexta

2. **Breast Cancer franchise**
   - TNBC: Tecentriq, ipatasertib
   - HR+: SERD (RG6171), PI3Kα (RG6114)
   - HER2+: Tecentriq

3. **Lung Cancer franchise**
   - NSCLC: Tecentriq, tiragolumab
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Port Delivery System (PDS)
Potential to improve real world outcomes with twice yearly dosing

Adherence to IVT therapies is low and infrequent dosing in the real world correlates with vision loss

Only 50% of patients can be extended to Q3M dosing with current IVT therapies

With PDS, nearly all patients can be maintained on 6m dosing, improving patient compliance and real world outcomes

• **PDS implant**: permanent, refillable intraocular implant. One-time ~30 min outpatient surgical procedure. Patients from Ph I study have had PDS implanted for >10 years.

• **Refill exchange**: twice yearly in-office refill of the device using proprietary needle assembly. Can only be refilled with proprietary formulation (not other molecules or biosimilars)
PDS efficacy equivalent to monthly Lucentis for nearly all patients

Strong patient preference for PDS

**Equivalent vision**

Adjusted mean BCVA change from baseline

Adjusted mean BCVA change from baseline. The graph shows a trend line with error bars indicating the range of mean BCVA change. The line is flat with a slight upward trend, suggesting minimal change over time.

**Treatment durability**

Percentage of PDS patients who received supplemental treatment before first refill-exchange at week 24

The graph shows the percentage of PDS patients who received supplemental treatments before the first refill-exchange. The percentage is 98.4%, with 1.6% of patients receiving 1 to 3 supplemental treatments.

**Patient preference**

Preference among patients in the PDS arm at week 40

The pie chart indicates a high preference for PDS, with 93.2% of patients preferring PDS, 1.3% preferring intravitreal injections, and 5.6% showing no preference.

BCVA, best-corrected visual acuity; PDS, Port Delivery System with ranibizumab
Preparing for a purposeful global launch in nAMD
US launch planned for 2021, ex-US for 2022

Virtual reality training
- Virtual reality (VR) technology enables preoperative training of surgeons on PDS procedures (implant insertion and refill)
- >200 US surgeons trained in Ph III across ~100 sites

Field-based support
- Surgical Device Liaisons (SDLs) support training on site, and facilitate peer to peer discussion and education
- Focus on ensuring consistency in outcomes and enhancing the patient experience

Remote vision monitoring
- App-based designed test to detect changes in vision in-between office visits
- Vision alerts sent to doctor
- Pilot programs underway

Global retina market growing to ~$14b by 2024

nAMD = neovascular age related macular degeneration
# Neuroscience and Rare Diseases

## 1. Hematology franchise
- DLBCL: Polivy, glofitamab, mosunetuzumab
- FL: mosunetuzumab, glofitamab, Polivy
- AML: Venclexta
- MM: Venclexta
- MDS: Venclexta

## 2. Breast Cancer franchise
- TNBC: Tecentriq, ipatasertib
- HR+: SERD (RG6171), PI3Kαi (RG6114)
- HER2+: Tecentriq

## 3. Lung Cancer franchise
- NSCLC: Tecentriq, tiragolumab
- SCLC: Tecentriq, tiragolumab
- ALK+: Alecensa
- ROS1+/NTRK+: Rozlytrek
- RET+: Gavreto
- KRAS G12C+: GDC-6063

## 4. Other oncology
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- Thyroid cancer: Gavreto
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- Hemophilia A: Hemlibra
- Hemophilia A: Factor VIII Gene Therapy
- PNH: crovalimab

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- MS: Ocrevus; fenebrutinib
- SMA: Evrysdi
- NMOSD: Enspryng
- AD: gantenerumab, anti-Tau, brain shuttle
- Huntington’s disease: tominersen
- DMD: Micro-dystrophin Gene Therapy
- Parkinson’s disease: prasinezumab

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- IPF: rhPentaxin-2, Esbriet
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- Influenza A/B: Xofluza
- SARS-CoV2: Actemra
- SARS-CoV2: REGN-COV2

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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 20 results presentation appendix or visit the IR homepage.
Ocrevus: Best in disease efficacy with robust, consistent, and sustained delay in disability progression

- 46% lower risk of requiring a walking-aid in those patients who initiated OCR earlier vs delayed treatment (those switching from IFN β-1a)
- 44% lower risk of requiring a wheelchair in those patients who initiated OCR earlier vs delayed treatment (those switching from PBO)
- ~35% of US sales in PPMS

>170K patients treated with consistent and favorable benefit risk profile

Ocrevus twice yearly dosing drives better compliance

### Total Yearly Dosing

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosing</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCREVUS</td>
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<tr>
<td>TECFIDERA</td>
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<tr>
<td>AUBAGIO</td>
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<tr>
<td>TYSABRI</td>
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<tr>
<td>COPAXONE</td>
<td>x365</td>
<td>(or 156)</td>
</tr>
<tr>
<td>KESIMPTA</td>
<td>x12</td>
<td></td>
</tr>
</tbody>
</table>

>90% persistence/adherence after 1 yr; superior to oral and injectable medicines

- Superior persistence and adherence and the lowest discontinuation rate at both 12 and 18 months of follow-up compared with patients initiating other classes of MS DMTs
- Persistence and adherence to treatment are critical for achieving therapeutic goals in MS

*Total yearly dosing after the first year; DMT = disease modifying therapy
Continuing to improve patient convenience with shorter infusion

Favorable access with no price increases since launch

<table>
<thead>
<tr>
<th>Ocrevus short infusion nearly halves administration time</th>
<th>Ocrevus pricing in US results in broad access</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional Infusion 3.5 hours</td>
<td>$65k per year</td>
</tr>
<tr>
<td>Shorter infusion 2 hours</td>
<td>• Priced ~32% below US market average WAC of $94k</td>
</tr>
<tr>
<td></td>
<td>• &gt;80% RMS and 98% PPMS covered without step edits</td>
</tr>
</tbody>
</table>

Approved by EMA, FDA approval expected before end of the year

Expansion in infusion options for patients

• Ocrevus has been infused in >46K locations in the US
• ~50% of infusions occur outside of the hospital

Total time requires pre-medication (30min-1hr and observation 1hr), *home administration in certain markets
Enspryng: First and only subcutaneous treatment for NMOSD

Significant unmet need still exists with NMOSD

- 200K patients worldwide
- 70-80% of patients are AQP4+
- Half of patients are blind or require a wheelchair within 5 yrs
- 40% of patients with NMOSD are first misdiagnosed as having MS
- 50% of patients treated with steroids/immunosuppressants

Approved in US, Canada, Japan, Switzerland
Additional applications are under review including the EU and China

✔ Highly effective
  - Comparable efficacy to best in disease treatments

✔ Flexible and convenient
  - Q4w SC dosing at home
  - Studied as monotherapy and in combination with immunosuppressants

✔ Well tolerated safety profile
  - No black box warning; lower rate of infections incl. serious infections than placebo group

✔ Competitively priced
  - Priced 72% below eculizumab and 27% below inebilizumab after first year
Evrysdi
Proven efficacy in infants, children and adults with SMA

Best-in-class efficacy and safety potential
Durably increases SMN protein in CNS and periphery
Out of 450+ patients studied, none withdrew from treatment due to treatment-related AEs

Broad population studied
Newborn to 60 years old, Type 1/2/3, naïve and pre-treated
Real world population that exhibits a broad range of disease severity & functional ability

Advantages of oral administration
Oral liquid solution, administered at home
Delivered directly to patient, with contactless delivery

* Based on the average infant weight from the FIREFISH trial
Evrysdi: Evidence being generated across all SMA patients
Representative range of ages, type, prior treatment, disease severity

<table>
<thead>
<tr>
<th>Presymptomatic Newborns</th>
<th>Symptomatic Infants</th>
<th>Younger Children</th>
<th>Older Children</th>
<th>Teenagers</th>
<th>Adults</th>
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<tbody>
<tr>
<td>RAINBOWFISH</td>
<td>FIREFISH</td>
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<td>SUNFISH</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>JEWELFISH</td>
<td></td>
</tr>
</tbody>
</table>

- ≤ 5 years old
- > 5 years old
- ~15% prevalence*
- ~85% prevalence*

Focus of many recent trials in SMA
Large prevalent population that remains underserved lacking treatment options and supporting evidence

The majority of patients are not receiving disease modifying therapy

* Estimated 2020 prevalence in US and EU5
Successful virtual launch of Evrysdi in the US
SMA patients being treated across all segments

**Broad uptake across segments in first month of approval**

- **Patients treated with all SMA types**
  ~25% of patients with Type I SMA

- **Treatment naïve and switch patients**
  Have treated pts switching from both Spinraza / Zolgensma

- **Broad range of ages**
  5m old infants to 70+ year old adults

**Access supported by responsible pricing**

- **25% discount** to current SOC over 5-yrs (at max Evrysdi price)

- **Infants**
  <$100K / year
  15lbs/7kg (~2 yrs old)*

- **Maximum Price**
  $340k / year
  >44lbs/20kg (~6 yrs old)

- **No additional administration costs**
- **Commercial and state Medicaid plans moving fast to establish coverage policies**

* Based on the average infant weight from the FIREFISH trial
Rare diseases present significant opportunity in China

Large populations of patients with rare diseases

- China was the #1 enrolling country in FIREFISH Part II trial
- Regulatory submission completed in China with approval expected H1 2021
- Enspryng China filing dossier accepted with priority review
- NMOSD included on China Rare Disease List
- NRDL negotiations for Inhibitor expected in 2020
- Regulatory submission completed for Non-Inhibitor label expansion with approval expected in H1 2021

Source: McKinsey Report
Closing the approval gap in China
Bringing innovative medicines to Chinese patients faster

NRDL negotiations expected in 2020 for Kadcyla, Tecentriq, Hemlibra

3-5x volume growth seen with other Roche medicines within 2 years of addition to NRDL

Tecentriq+Avastin 1L HCC approval expected in 2020 (within 5-6 months of US approval)

NRDL: National Reimbursed Drug List; 2 Refers to Avastin Lung Cancer Indication; 3 Refers to Kadcyla Early Breast Cancer Indication; 4 Refers to Tecentriq Small Cell Lung Cancer Indication
### Strong short- and mid-term news flow

*Diversifying the late stage pipeline and setting new standards of care*

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication</th>
<th>Filing</th>
<th>Market potential</th>
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<tbody>
<tr>
<td>tominersen</td>
<td>Huntington’s</td>
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<tr>
<td>gantenerumab</td>
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<td>SRP-9001</td>
<td>DMD</td>
<td>latest 2023</td>
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<td>nAMD DME</td>
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<tr>
<td>faricimab</td>
<td>DME nAMD</td>
<td>2021</td>
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<tr>
<td>Actemra + remdesivir</td>
<td>COVID-19</td>
<td>2021</td>
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<tr>
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<th>Product</th>
<th>Indication</th>
<th>Filing</th>
<th>Market potential</th>
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<tbody>
<tr>
<td>Gavreto</td>
<td>RET+ NSCLC</td>
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<td></td>
<td>thyroid cancer</td>
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<tr>
<td>Tecentriq</td>
<td>NeoAdj TNBC</td>
<td>2020</td>
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<tr>
<td></td>
<td>Adj SCCHN</td>
<td>2021</td>
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<td></td>
<td>Adj RCC</td>
<td>2021</td>
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<tr>
<td></td>
<td>(Neo)Adj NSCLC</td>
<td>2021/22</td>
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<tr>
<td></td>
<td>Adj HCC</td>
<td>2022</td>
<td></td>
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<tr>
<td>Tecentriq + P+H</td>
<td>NeoAdj HER2+ BC</td>
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<td>ipatasertib</td>
<td>1L/2L TNBC</td>
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<tr>
<td></td>
<td>1L mCRPC</td>
<td>2020</td>
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<tr>
<td>Polivy</td>
<td>1L DLBCL</td>
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<tr>
<td>tiragolumab + T</td>
<td>1L SCLC</td>
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<tr>
<td>mosunetuzumab</td>
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<td>2021</td>
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<tr>
<td>glofitamab</td>
<td>R/R DLBCL</td>
<td>2022</td>
<td></td>
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<tr>
<td>Venclexta</td>
<td>R/R MM t(11;14)</td>
<td>2022</td>
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</tr>
<tr>
<td>SERD (RG6171)</td>
<td>2L/3L mBC</td>
<td>2022</td>
<td></td>
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</table>

Source: Roche/Genentech, incidence/prevalence in the major markets (US, FR, DE, IT, ES, GB); DMD=duchenne muscular dystrophy; nAMD=neovascular age-related macular degeneration; DME=diabetic macular edema; NSCLC=non-small cell lung cancer; TNBC=triple-negative breast cancer; SCCHN=squamous cell carcinoma of the head and neck; RCC=renal cell carcinoma; HCC=hepatocellular carcinoma; mCRPC=metastatic castration resistant prostate cancer; DLBCL=diffuse large B-cell lymphoma; SCLC=small cell lung cancer; FL=follicular lymphoma; PNH=paroxysmal nocturnal hemoglobinuria
short break
Roche Late Stage Pipeline Event 2020

Late Stage Pipeline Oncology & Non-malignant Hematology

Levi Garraway, M.D., Ph.D. | Executive Vice President, Head of Global Product Development and Chief Medical Officer
**Late stage pipeline update**

1. **Hematology franchise**
   - DLBCL: Polivy, glofitamab, mosunetuzumab
   - FL: mosunetuzumab, glofitamab, Polivy
   - AML: Venclexta
   - MM: Venclexta
   - MDS: Venclexta

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   - TNBC: Tecentriq, ipatasertib
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   - CRPC: ipatasertib
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   - Melanoma: Tecentriq, Cotelic, Zelboraf

5. **Non-malignant hematology**
   - Hemophilia A: Hemlibra
   - Hemophilia A: Factor VIII Gene Therapy
   - PNH: crovalimab

6. **Neuroscience**
   - MS: Ocrevus; fenebrutinib
   - SMA: Evrysdi
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   - Myelofibrosis: rhPentraxin-2
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   - Crohn’s disease: etrolizumab

8. **Ophthalmology**
   - nAMD, DME, DR: Port Delivery System
   - nAMD, DME, RVO: faricimab

9. **Infectious diseases**
   - HBV: TLR7 agonist, CpAM, RG6346, RG6084
   - Influenza A/B: Xofluza
   - SARS-CoV2: Actemra
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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 20 results presentation appendix or visit the IR homepage*
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Hematology: Glofitamab in NHL
Potential for early filing in R/R DLBCL

• The ≥10mg cohorts in R/R aNHL showed an ORR of 49.4% and a CR rate of 34.1%; CRs appeared durable with the mDOR not reached after a median follow up of 10.2m
• Good safety profile with manageable CRS confined to cycle 1
• Combination development with R-CHOP and Polivy in DLBCL on-going
• Ph III safety run-in for glofitamab + GemOx in 2L+ DLBCL initiated

Dickinson. M.J. et al, EHA 2020; aNHL=aggressive non-Hodgkin’s lymphoma; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; glofit=glofitamab; GemOx=gemcitabine, oxaliplatin; G=Gazyva; R-CHOP=Rituxan, cyclophosphamide, doxorubicin, vincristine, prednisone; P=Polivy; ORR=overall response rate; CR=complete response; mDOR=median duration of response; CRS=cytokine release syndrome; *Aggressive NHL includes primarily DLBCL, some transformed FL, PMBCL, MCL, transformed MZL and Richter’s transformation.
Hematology: Exploring feasible combinations

Initial efficacy and safety data show combination potential

**Ph I results of glofitamab + Tecentriq in R/R NHL**

- T-cell activation observed consistent with the hypothesized MOA of the combination
- Trend towards increased response rate was observed starting at glofitamab doses ≥1.8mg
- Manageable safety in R/R NHL

**Ph I results of glofitamab + Gazyva in R/R NHL**

- Highly promising activity in heavily pre-treated patients
- ORR and CR rates by investigator assessment were 54% (15/28 pts) and 46% (13/28); CR appear durable
- Safety profile consistent with known safety profiles of the individual drugs

Further development work needed to identify most promising paths forward for chemo-free combinations

Hematology: Mosunetuzumab in NHL
Potential for early filing in R/R FL; SC data to be presented at ASH

**CD20 x CD3 program**

- **Combination**
  - mosun+len
  - mosun+CHOP *
  - mosun+CP+P
  - mosun *
  - mosun *
  - mosun *
  - mosun + P
  - mosun + T
  - mosun SC *

- **Indication**
  - R/R FL
  - 1L DLBCL
  - 1L DLBCL
  - R/R DLBCL/MCL
  - 1L/2L (unH) DLBCL
  - 3L + DLBCL/FL/ibrutinib R/R MCL
  - R/R DLBCL
  - R/R DLBCL
  - R/R DLBCL/FL

- **Phase**
  - Ph1
  - Ph2
  - Ph3

**Mosunetuzumab in 3L+ FL**

- **Tumor responses**

- **Combination**
  - mosun+len
  - mosun+CHOP *
  - mosun+CP+P
  - mosun *
  - mosun *
  - mosun *
  - mosun + P
  - mosun + T
  - mosun SC *

- **Indication**
  - R/R FL
  - 1L DLBCL
  - 1L DLBCL
  - R/R DLBCL/MCL
  - 1L/2L (unH) DLBCL
  - 3L + DLBCL/FL/ibrutinib R/R MCL
  - R/R DLBCL
  - R/R DLBCL
  - R/R DLBCL/FL

- **Data submitted to ASH 2020**

- **• Pooled data from 2.8mg to 13.5mg cohorts showed an ORR of 62.7% and CR of 43.3%; 82.8% patients remain in complete remission for up to 26m off initial treatment**
- **• Overall CRS rate of 28.9% (predominantly fever Gr1) with only 1.1% CRS events of Gr≥3**
- **• Ph III safety run-in for mosunetuzumab + lenalidomide in R/R FL initiated**
- **• First Ph I data on mosunetuzumab SC to be presented at ASH 2020**

Shuster, S.J., et al., ASH 2019; NHL=non-Hodgkin's lymphoma; DLBCL=diffuse large B cell lymphoma; FL=follicular lymphoma; CHOP=cyclophosphamide, doxorubicin, vincristine, prednisone; P=Polivy; T=Tecentriq; mosun=mosunetuzumab; ORR=overall response rate; CR=complete response; CRS=cytokine release syndrome; R/R=relapsed/refractory; mDOR=median duration of response; SC=subcutaneous
Hematology: Venclexta in CLL, AML, MM, MDS

Ph III studies to be initiated in various indications

Venclexta program

Bcl-2 inhibitor

<table>
<thead>
<tr>
<th>Combination</th>
<th>Indication</th>
<th>Ph1</th>
<th>Ph2</th>
<th>Ph3</th>
</tr>
</thead>
<tbody>
<tr>
<td>V+P+R</td>
<td>R/R DLBL-FL</td>
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</tr>
<tr>
<td>V+G</td>
<td>1L unfit CLL</td>
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<tr>
<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+R+R</td>
<td>R/R CLL after bone marrow</td>
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<td>V+G</td>
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<td>V+R+R</td>
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<tr>
<td>V+G+R</td>
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</tr>
</tbody>
</table>

Overall survival

- Ph III (Viale-A) results in 1L unfit AML filed in US (RTOR) and EU
- Ph III (Viale-M) in 1L fit AML initiated
- Ph III (CristaLLo) in 1L fit CLL with MRD as primary endpoint started in Q2 2020
- Additional Ph III studies in AML and MDS planned

DiNardo C.D. et al., EHA 2020; NHL=non-Hodgkin’s lymphoma; CLL=chronic lymphoid leukemia; AML=acute myeloid leukemia; MM=multiple myeloma; MDS=myelodysplastic syndrome; mOS=median overall survival; HR=hazard ratio; V=Venclexta; P=Polivy; G=Gazyva; R=Rituxan; dex=dexamethasone; bor=bortezomib; aza=azacitidine; LDAC=low dose cytarabine; RTOR=real-time oncology review; Venclexta in collaboration with AbbVie
Late stage pipeline update

1. Hematology franchise
   - DLBCL: Polivy, grofitamab, mosunetuzumab
   - FL: mosunetuzumab, grofitamab, Polivy
   - AML: Venclexta
   - MM: Venclexta
   - MDS: Venclexta

2. Breast Cancer franchise
   - TNBC: Tecentriq, ipatasertib
   - HR+: SERD (RG6171), PI3Kαi (RG6114)
   - HER2+: Tecentriq

3. Lung Cancer franchise
   - NSCLC: Tecentriq, tiragolumab
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   - ROS1+/NTRK+: Rozlytrek
   - RET+: Gavreto
   - KRAS G12C+: GDC-6063

4. Other oncology
   - CRPC: ipatasertib
   - Thyroid cancer: Gavreto
   - Esophageal cancer: tiragolumab
   - Melanoma: Tecentriq, Cotelic, Zelboraf

5. Non-malignant hematology
   - Hemophilia A: Hemlibra
   - Hemophilia A: Factor VIII Gene Therapy
   - PNH: crovalimab

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   - MS: Ocrevus; fenebrutininib
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   - NMOSD: Enspryng
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   - nAMD, DME, DR: Port Delivery System
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   - HBV: TLR7 agonist, CpAM, RG6346, RG6084
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   - SARS-CoV2: REGN-COV2

* For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 20 results presentation appendix or visit the IR homepage.
TNBC franchise: Tecentriq + nab-pac new SOC in 1L

Positive Ph III results in neoadjuvant

Ph III (IMpassion130) results in 1L

Clinically meaningful OS improvement (2nd interim)
PDL1+ population

Stratified HR = 0.71* (95% CI: 0.54, 0.94)

Delta 7 mo

18.0 mo (13.6, 20.1)

25.0 mo (19.6, 30.7)

TNBC program covering all lines of treatment*

• Positive Ph III (IMpassion031) results for Tecentriq+nab-pac in neoadjuvant TNBC announced; data to be presented

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
HR+/HER2- franchise: Potentially best in class 3rd gen SERD

Strong efficacy as a single agent and in combination

Selective ER degrader (SERD)
RG6171 (GDC-9545)

- 3rd generation oral SERD
- Highly potent in vitro and improved efficacy in vivo versus previous SERDs
- High potency + minimal safety findings lead to wide nonclinical safety margins
- First SERD with positive combination data with a CDK4/6 inhibitor

Ph Ib results: Tumor responses RG6171 +/- palbociclib

- Strong potentially best-in-class efficacy as single agent or in combination with a CDK4/6 inhibitor in pre-treated ER+ patients, regardless of ESR1 resistance mutations
- Well-tolerated up to doses of 100 mg daily
- Expansion cohort at 30 mg daily on-going given the promising efficacy with a clinical benefit rate of 50%*

Lim E. et al., ASCO 2020; Metcalfe C. et al., SABCS 2018; HR=hormone receptor; mBC=metastatic breast cancer; ER=estrogen receptor; LHRH=lutenizing hormone /releasing hormone; * At 30 mg no bradycardia events reported to date
HR+/HER2- franchise: Potentially best in class 3rd gen SERD
Ph III program in 1L+ and eBC initiated

3rd gen SERD: Overcoming fulvestrant limitations
Improved MOA for a well established target

- RG6171 is a 3rd generation SERD with improved bioavailability and a novel MOA: Increased efficacy is due to “ER immobilization” which suppresses transcriptional activity prior to ER degradation

Ph III trial design in 1L mBC

- Ph III RG6171 + palbociclib in 1L mBC to start in 2H 2020
- Ph II RG6171 + palbociclib in neoadjuvant started in Q3 2020; Ph III adjuvant study planned
- Pivotal Ph II RG6171 in 2/3L to start in Q4 2020; results expected in 2022
HR+/HER2- franchise: PI3Kα in PIK3CA-mutant tumors

Ph III for potentially best in class PI3Kα inhibitor started

**PI3Kα selective inhibitor + mutant PI3Kα degrader**

- Dual MOA: More potent and selective for PI3Kα + degrades mutant PI3Kα
- Greater safety margins
- Better in vivo efficacy
- Greater, more durable target inhibition
- Combinations with other therapies

**Ph I (dose escalation and expansion cohort)**

- Strong efficacy in on-going Ph I/Ib as single agent or as combo with ET (letrozole or fulvestrant) +/- palbociclib in patients with locally advanced or metastatic PIK3CA-mutant solid tumors
- Good safety as single agent or combined
- Ph III (INAVO120) RG6114* + palbociclib + fulvestrant in 1L PIK3CA-mutant HR+/HER2- mBC started in Q1 2020

Jhaveri, K., et al, SABCS 2019; Kalinsky K. et al., AACR 2020; ET=endocrine therapy; HR=hormone receptor; BC=breast cancer; ORR=overall response; * GDC-0077
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Lung franchise
Integrated value proposition for patient classification & care

Evolution of lung cancer classification

- Roche uniquely positioned to establish integrated PHC solutions
- Develop rare mutation agents faster and cheaper leveraging B-FAST, FMI, Flatiron, PHC
- Multiple lung pilots focused on integrated offerings underway (Taiwan, Croatia, Australia)

Lung franchise: Overview adjuvant program
NSCLC, HER2+ BC, SCCHN reading out in 2021
Lung franchise: Tiragolumab + Tecentriq in NSCLC & SCLC

Pivotal Ph III study in stage III NSCLC initiated

**Anti-TIGIT mAb**

- Fully human IgG1/kappa Ab with intact Fc region that blocks the binding of TIGIT to its receptor PVR
- Could restore anti-tumor response and could complement the activity of anti-PD-L1/PD-1 antibodies

**Randomized Ph II (CITYSCAPE) in 1L NSCLC**

- Tiragolumab + Tecentriq showed clinically meaningful improvement in ORR and PFS in the ITT population with a greater magnitude of improvement in the PD-L1 TPS ≥ 50% subgroup
- Tiragolumab + Tecentriq was well-tolerated with a safety profile similar to the control arm
- Ph III in 1L PDL1+ NSCLC (SKYSCRAPER-01), 1L ES-SCLC (SKYSCRAPER-02) and stage III NSCLC (SKYSCRAPER-03) on-going
- Ph II (CITYSCAPE) update including OS in 2021

Johnson et al. Cancer Cell 2014; Rodriguez-Abreu D. et al., ASCO 2020; Follow-up data cut-off: 02 December, 2019; Ab=antibodies; ORR=overall response rate; PFS=progression free survival; HR=hazard ratio; NE=non evaluable; ITT=intention-to-treat; TPS=tumor proportion score; ES-SCLC=extensive stage SCLC; OS=overall survival; * unstratified HR
Lung franchise: Gavreto new SOC in RET+ mNSCLC
Strong and durable responses including CNS disease control

RET inhibitor

• Oral small molecule kinase inhibitor
• Highly selective for RET fusions and mutations, including predicted resistance mutations
• Brain penetrant and CNS active
• ~1-2% of NSCLC patients with RET fusions, thereof ~40% with brain metastases

Ph I/II (ARROW) results in RET fusion+ mNSCLC

Tumor responses

• 70% ORR in naive including 11% CR and 57% ORR in post-platinum patients including 6% CR*
• CNS ORR at 56% (n=9) including 33% CR; rapid and durable responses; mDOR not reached
• Well-tolerated across tumor types with most AEs of grade 1–2
• Ph III (AcceleRET Lung) in 1L advanced or metastatic RET+ NSCLC on-going
• US accelerated approval in RET+ mNSCLC achieved in Q3 2020; filed in the EU

CNS responses

Gainor J. F. et al, ASCO 2020

\*Data in the label; SOC=standard of care; CNS=central nervous system; BTD=break through designation; mNSCLC=metastatic non small cell lung cancer; MTC=medullary thyroid cancer; ORR=overall response rate; CR=complete response; mDOR=median duration of response; AE=adverse events; Gavreto (pralsetinib) in collaboration with Blueprint Medicines; Gavreto, Blueprint Medicines and associated logos are trademarks of Blueprint Medicines Corporation; Gavreto was discovered by Blueprint Medicines
Lung franchise: GDC-6036 (KRAS G12C inhibitor) in solid tumors

G12C driver mutations found in 12% of all NSCLC patients

- Highly potent irreversible covalent inhibitor of the KRAS G12C mutant protein, which becomes locked in an inactive state
- Minimal safety findings leading to wide nonclinical safety margins

- GDC-6036 causes tumor growth inhibition in multiple patient derived KRAS G12C+ cell lines and in xenograft mouse models
- GDC-6036 synergizes with multiple targeted therapies; strong scientific rationale for combining with medicines that act on other parts of RAS pathway to deepen responses, extend duration of disease control, and limit treatment resistance.
- Ph I dose escalation and expansion in KRAS G12C+ solid tumors started in Q2 2020
Lung franchise: Blood-based NGS ctDNA assays
30% of lung cancer patients with insufficient biopsy material

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

- Allows for serial liquid biopsy testing to follow tumor evolution and resistance
- RWD cohort paired with NGS testing provides additional natural history & epidemiological data
- Primary endpoint in the ALK+ cohort met; filed in Q1 2020

Blood based biomarkers

- Liquid biopsy test that detects the 4 main classes of genomic alterations (324 genes), bTMB, MSI
- Comprehensive genomic profiling including resistance mutations or fusions in NSCLC
- Guides therapy selection and clinical trials

Mok T. et al., WCLC 2017; NGS=next generation sequencing; ctDNA=circulating tumor DNA; RWD=real world data; bTMB=blood tumor mutational burden; MSI=microsatellite instability
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GU franchise: Ipatasertib in 1L mCRPC
Positive Ph III results for patients with PTEN loss

Highly selective AKT inhibitor

• Oral, highly specific inhibitor of all three activated isoforms of AKT and potentially preventing cancer cell growth and survival

• Clinical development in tumors with high frequency of PI3K/AKT pathway activation (CRPC, TNBC, HR+ mBC)

Ph II (A.MARTIN) results

<table>
<thead>
<tr>
<th>biomarker</th>
<th>PTEN loss</th>
<th>PTEN norm- loss</th>
<th>PTEN loss</th>
<th>PTEN norm- loss</th>
<th>PTEN loss</th>
<th>PTEN norm- loss</th>
<th>PTEN loss</th>
<th>PTEN norm- loss</th>
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<tbody>
<tr>
<td>IHC</td>
<td>11.5</td>
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<td>13.7</td>
<td>6.3</td>
<td>13.8</td>
<td>7.4</td>
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</tr>
<tr>
<td>Ventana</td>
<td>6.5</td>
<td>5.8</td>
<td>6.5</td>
<td>5.8</td>
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<td>FISH</td>
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<td>0.87</td>
<td>0.77</td>
<td>0.26</td>
<td>0.52</td>
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</tr>
<tr>
<td>NGS</td>
<td>0.22-0.30</td>
<td>0.53-1.37</td>
<td>0.29-0.87</td>
<td>0.41-1.32</td>
<td>0.38-1.28</td>
<td>0.30-0.69</td>
<td>0.25-1.33</td>
<td></td>
</tr>
</tbody>
</table>

Biomarker assay

Roche VENTANA PTEN (SP218)

• IHC detection of PTEN protein loss in formalin-fixed, paraffin-embedded tissue

• Strong concordance to DNA technologies (NGS and FISH)

Ph II: rPFS was prolonged in the ipatasertib 400 mg arm (8.2m vs 6.4m; HR=0.75); Dose-dependent improvement was observed in OS

• PTEN loss was associated with an improved rPFS outcome (HR of 0.39 at 400mg dose) as measured by NGS, FISH and IHC

• Ph III (IPATential150) met co-primary endpoint of rPFS in patients with PTEN loss

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; * unstratified HR; 90% CI
GI franchise: Tiragolumab in esophageal cancer (EC)

**Pivotal Ph III studies initiated**

**Ph III trial design (SKYSCRAPER-07)**

**in locally advanced EC**

- **Locally Advanced Esophageal**
  - All-comer
  - Definitive platinum-based chemotherapy and radiation therapy and no progression
  - ECOG PS 0-1
  - Squamous

<table>
<thead>
<tr>
<th></th>
<th>Ph III trial design (SKYSCRAPER-07) in locally advanced EC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Tecentriq (1200) + tiragolumab (600) q3w up to 12m (n=250)</td>
</tr>
<tr>
<td>B</td>
<td>Tecentriq (1200) + placebo q3w up to 12m (n=250)</td>
</tr>
<tr>
<td>C</td>
<td>Placebo + placebo q3w up to 12m (n=250)</td>
</tr>
</tbody>
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Randomized 1:1:1 within 1-42 days (TBD)

- 1EP: PFS A vs C; OS (hierarchical) A vs C; OS (hierarchical) B vs C
- 2EP: OS, PFS A vs B; PFS B vs C; ORR; DOR; safety; QoL

**Ph III trial design (SKYSCRAPER-08)**

**in 1L esophageal squamous cancers (ESCC)**

<table>
<thead>
<tr>
<th></th>
<th>Ph III trial design (SKYSCRAPER-08) in 1L esophageal squamous cancers (ESCC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Tecentriq (1200) + tiragolumab (600) + cisplatin + paclitaxel (n=225)</td>
</tr>
<tr>
<td>B</td>
<td>Placebo + placebo + cisplatin + paclitaxel (n=225)</td>
</tr>
<tr>
<td>C</td>
<td>Placebo + placebo</td>
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Until disease progression or unacceptable toxicity

- 1EP: OS, PFS
- 2EP: DOR; ORR; safety; QoL

- Preliminary Ph Ib safety and efficacy data in EC to be presented at upcoming conference
- Global development program with focus on Asia, especially China
- Ph III starts expected in 2020

Ab=antibodies; ORR=overall response rate; TPS=tumor proportion score; PFS=progression free survival; NE=non evaluable; ITT=intention-to-treat; * unstratified HR
Thyroid cancer franchise: Gavreto in RET+ TC
Excellent efficacy and durability across thyroid cancer types

**RET inhibitor**

- Oral small molecule kinase inhibitor
- Highly selective for RET fusions and mutations, including predicted resistance mutations
- Brain penetrant and CNS active
- 90% of advanced MTC patients with RET activating mutations and ~10-20% of PTC patients with RET fusions

**Ph I/II (ARROW) results**

- RET+ MTC: ORR 74% in naive patients and 60% ORR in pretreated patients; mDOR not reached *
- RET+ TC: 91% ORR and 6-month DOR stands at 100%
- Registrational data on Ph I/II (ARROW) MTC results to be presented at ESMO
- Ph III (AcceleRET MTC) in MTC to start in H2 2020
- US priority review and RTOR for advanced or metastatic RET+ thyroid cancer on-going

* MTC data released by Blueprint Medicines on April 1, 2020; Subbiah V, et al, ASCO 2020; SOC=standard of care; TC=thyroid cancer; MTC=medullary thyroid cancer; PTC=papillary thyroid cancer; CNS=central nervous system; BTD=breakthrough therapy designation; RTOR=real time oncology review; ORR=overall response rate; mDOR=median duration of response; Gavreto (pralsetinib) in collaboration with Blueprint Medicines; Gavreto, Blueprint Medicines and associated logos are trademarks of Blueprint Medicines Corporation; Gavreto was discovered by Blueprint Medicines
Melanoma franchise: Tecentriq + Cotellic + Zelboraf

First CIT+targeted therapy in BRAF V600+ melanoma

Ph III (IMspire150/TRILOGY) results in BRAF+ melanoma

- Statistically significant and clinically meaningful improvement in investigator-assessed PFS (HR=0.78; 15.1m vs 10.6m) and clinically meaningful improvement in mDOR (21.0m vs 12.6m); no new safety signals were identified
- OS data not mature but favored triplet; next interim expected H1 2021
- FDA approval granted in Q2 2020 under priority review and being part of FDA’s project Orbis

McArthur G.A. et al., AACR 2020; CIT=cancer immuno therapy; Atezo=atezolizumab (Tecentriq); CI=confidence interval; Cobi=cobimetinib (Cotellic); Pbo=placebo; Vem=vemurafenib (Zelboraf);
PFS=progression free survival; Cotellic in collaboration with Exelixis; Zelboraf in collaboration with Plexxikon
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Non-malignant hematology: RG6357 (SPK-8011) in hem A
Early efficacy and safety data after 2 to 3.3 years of follow-up

Hemophilia A gene therapy

- Bio-engineered adeno-associated viral (AAV) vector utilizing the AAV-LK03 capsid (Spark200)
- Contains a codon-optimized human factor VIII gene under the control of a liver-specific promoter

Ph I/II (SPK-8011) results

Annualized bleed rate (ABR) of participants with sustained expression (n=12)*

- Data from 5 participants in the 5x10^{11} and 1x10^{12} vg/kg dose cohorts and 7 participants in the 2x10^{12} vg/kg dose cohort showed a 91% ABR reduction and a 96% reduction in FVIII infusions
- The 5 participants in the 5x10^{11} and 1x10^{12} vg/kg cohorts demonstrated durable and stable FVIII expression, had a clinically significant reduction in bleeding and factor use and showed an acceptable safety profile for 2 to 3.3 years of follow up
- Further dose optimization and selection of immunomodulatory regimen on-going
- Ph III to be initiated in 2021

George, L.A. et al, ISTH 2020; * Excludes 2 participants who lost expression
Non-malignant hematology: Crovalimab in PNH
Recycling Ab for maximal inhibition of C5

Anti-C5 mAb

- Chugai engineered, anti complement component 5 (C5) recycling mAb\(^1\)–\(^6\)
- Engineered to enable maximal, long-lasting neutralization of C5 in complement mediated diseases
- Convenient SC Q4W dosing at home

Ph I/II (COMPOSER) results

- Ph I/II (COMPOSER) results show complete complement inhibition and a well-tolerated safety profile in C5i-naive patients and eculizumab pre-treated patients\(^1\)
- Efficacy was maintained over long-term treatment (44 patients treated for a median of 71 weeks) and breakthrough hemolysis events were infrequent\(^7\)
- Ph III switch and naive studies (COMMODORE 1/2) in PNH to start in 2020
- Development in additional complement-mediated diseases is being explored

Clinico-Genomic Database
Combining RWD and genomics drives R&D

Database R&D applications:
- Understanding genomics of rapidly progressive disease
- Natural history cohorts for defined populations (ALK, NTRK, EGFR, ROS-1, RET, KRAS, etc.), including patterns of metastatic spread
- Mechanisms of resistance
- Improved prognostic classifiers

Recent R&D examples:
- Analysis found cumulative incidence of brain metastases in patients with a certain mutation is significantly higher than in patients with wild-type allele or other mutations; decision to develop brain-penetrant molecule as part of the broader development strategy
- Analysis of CGDB used to decipher a molecular mechanism for checkpoint inhibitor resistance and ultimately helped address a fundamental question that can potentially benefit many cancer immunotherapy projects

Linking advanced tumor genetics with clinical outcomes drives scientific hypothesis generation

RWD = real world data; CGDB = Clinico-Genomic Database
Our technology platforms keep expanding*

<table>
<thead>
<tr>
<th>Small molecules</th>
<th>Bi-specifics</th>
<th>Fusion protein</th>
<th>mAb</th>
<th>Antibody drug conjugate</th>
<th>Personalized mRNA vaccine</th>
<th>Personalized T cells</th>
<th>RNA technologies</th>
<th>Gene therapy</th>
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<td>iNeST platform: mRNA-LPX Liposome</td>
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<td>Gavreto</td>
<td>mosunetuzumab</td>
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<td>SPK-8011</td>
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<tr>
<td>RG6114</td>
<td>Her2 x CD3</td>
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<td>KRAS G12C</td>
<td>FcRh5 x CD3</td>
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<td>Target oncogenes, induce apoptosis, suppress tumor growth</td>
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<thead>
<tr>
<th></th>
<th>mAb</th>
<th>Fusion protein</th>
<th>inNeST = Individualized Neoantigen-Specific Therapy</th>
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<tbody>
<tr>
<td>FAP x IL2v</td>
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<td>tiraogolumab</td>
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<td>codituzuamab</td>
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<td>Polivy</td>
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<td>iNeST</td>
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<td>Patient's neo-antigens for anti-tumour immune response</td>
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<td>Targeted toxic payload</td>
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<td>Amply immune response</td>
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<tr>
<th>Recombinant proteins</th>
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<tr>
<td>Evrnydil</td>
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<td>fenebrutinib</td>
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<td>TLR7 agonist</td>
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<td>GABA Aα5 PAM</td>
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<td>PTH1R agonist</td>
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<td>Hemlibra</td>
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<td>FGFR1 x KLB</td>
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<tr>
<td>brain shuttle</td>
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<td>Anti-S. aureus TAC</td>
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</tbody>
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* List of pipeline and launched molecules shown is not complete; iNeST = Individualized Neoantigen-Specific Therapy
Roche Late Stage Pipeline Event 2020

Late Stage Pipeline Neuroscience

Paulo Fontoura, M.D. Ph.D. | Senior Vice President, Global Head Neuroscience and Rare Diseases Clinical Development
**Neuroscience and rare diseases portfolio**

**Strongly differentiated pipeline**

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### Phase 1 (5 NMEs)
- **RG6102**
  - brain shuttle
gantenerumab
  - Alzheimer’s

- **RG7816**
  - GABA
t (5 PAM)
  - Autism spectrum disorder

- **RG7637**
  - undisclosed

- **RG6091**
  - UBE3A-LNA
  - Angelman syndrome

- **RG6237**
  - undisclosed

---

### Phase 2 (3 NMEs)
- **RG7935**
  - prasinezumab
  - Parkinson's

- **RG6100**
  - semorinemab
  - (anti-Tau)
  - Alzheimer's

- **RG7906**
  - ralmitaront
  - Schizophrenia

---

### Late Stage (4 NMEs)
- **RG1450**
  - gantenerumab
  - Alzheimer’s

- **RG6042**
  - tominersen
  - Huntington’s

- **SRP 9001**
  - microdystrophin RD gene therapy
  - DMD

- **RG7845**
  - fenebrutinib
  - MS

---

### Launched (3)
- **RG1594**
  - Ocrevus
  - MS

- **RG7916**
  - Enspryng
  - (satralizumab)
  - NMOSD

- **RG7916**
  - Evrysdii
  - (risdiplam)
  - SMA type 1/2/3

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- ✔️ FDA approval in 2020
- RD = Rare Diseases

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Risdiplam is developed in collaboration with PTC therapeutics and the SMA Foundation. Tominersen (ASO HTT) is developed in collaboration with Ionis Pharmaceuticals; ALS= Amyotrophic lateral sclerosis; NMOSD = neuromyelitis optica spectrum disorders; DMD= Duchenne muscular dystrophy; MS= Multiple sclerosis.
Late stage pipeline update

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   - RET+: Gavreto
   - KRAS G12C+: GDC-6063

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   - Hemophilia A: Factor VIII Gene Therapy
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   - Influenza A/B: Xofluza
   - SARS-CoV2: Actemra
   - SARS-CoV2: REGN-COV2

* For further information on target patient populations please consult the appendix; For further details on the late stage pipeline please consult the HY 20 results presentation appendix or visit the IR homepage.
MS franchise: Ocrevus shifting the standard of care
Robust, consistent, sustained impact on slowing disability progression

RMS: Ph III (OPERA) 6.5-year follow-up

- Reaching EDSS score ≥6.0, a key clinical disability milestone representing the requirement of a walking aid, which is associated with increased patient and societal burden

PPMS: Ph III (ORATORIO) 7-year follow-up

- Reaching EDSS score ≥7.0, a key clinical disability milestone representing wheelchair confinement, has a major impact on patients’ quality of life and associated treatment costs

RMS patients on Ocrevus over 6.5 yrs had a 46% reduction in the risk of needing a walking aid vs those who switched over from IFN β-1α treatment at the end of the double-blind period (p=0.004)

PPMS patients on Ocrevus over 7 yrs had a 44% reduction in the risk of needing a wheelchair (EDSS) vs those who switched over from IFN β-1α treatment at the end of the double-blind period (p=0.006)

Higher Ocrevus exposure was associated with lower B-cell levels and with greater control of disability progression without impacting safety.
MS franchise: Higher dose Ocrevus
New Ph III program in RMS and PPMS planned to start in 2020

Ph III study design for Ocrevus higher dose versus 600 mg in RMS and PPMS

- Ocrevus showed a significant benefit on 12/24W-CDP, ARR, MRI measures in Ph III studies in RMS and PPMS and 7 year OLE
- Exposure/response analysis suggests a higher dose could further lower the risk of disability progression without compromising safety
- Two double-blind, randomized Ph III studies designed to test higher dose Ocrevus; selected higher dose, given every 24 weeks, is 1,200 mg for patients <75 kg or 1,800 mg for patients ≥75 kg
- Ph III (MUSEtte) in RMS and Ph III (GAVotte) in PPMS to start in 2020

Hauser S.L. et al, ACTRIMS-ECTRIMS 2020; 24W-CDP=24 week confirmed disability progression; AAR=annual relapse rate; MRI=magnetic resonance imaging; RMS=relapsing multiple sclerosis; PPMS=primary progressive MS; OLE=open label extension
**MS franchise: Fenebrutinib in MS**

**Highly differentiated and potentially best-in-class BTKi in MS**

**BTK inhibitor**

<table>
<thead>
<tr>
<th>Fenebrutinib (See Ref)</th>
<th>Ibrutinib</th>
<th>Telebrutinib</th>
<th>Evobrutinib</th>
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<tbody>
<tr>
<td>Phase 3</td>
<td>Phase 3</td>
<td>Phase 3</td>
<td>Phase 3</td>
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<tr>
<td><strong>MS</strong></td>
<td>Oncology</td>
<td>MS</td>
<td>MS</td>
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<tr>
<td><strong>Noncovalent, reversible</strong></td>
<td><strong>Covalent, irreversible</strong></td>
<td><strong>Covalent, irreversible</strong></td>
<td><strong>Covalent, irreversible</strong></td>
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<tr>
<td>BTK IC50 2 nM</td>
<td>1 nM</td>
<td>1 nM</td>
<td>32 nM</td>
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<tr>
<td><strong>High selectivity</strong></td>
<td>Low selectivity</td>
<td>Low selectivity</td>
<td>Low selectivity</td>
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</table>

**Molecular and biological characterization**

- Oral, highly selective and only reversible noncovalent BTK inhibitor
- Long residence time bound to BTK mimics the durable inhibition of a covalent inhibitor but without the safety risks of covalent BTK inhibition

- Fenebrutinib’s BTK inhibition potential and kinase selectivity were assessed in a panel of 219 human kinases. Fenebrutinib was found to be highly BTK selective over other kinases which may reduce off target effects and improve safety
- Dual MOA: Fenebrutinib was shown to potently inhibit B cell and myeloid cell (macrophages, microglia) activation in whole human blood and thus may reduce both acute and chronic inflammation in MS, simultaneously

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Johnson A. et al, ACTRIMS-ECTRIMS 2020; MS=multiple sclerosis; BTK=Bruton’s tyrosine kinase; nM=nano molar; FACS=fluorescence-activated cell sorting
MS franchise: Fenebrutinib in MS
Ph III program to assess disease progression in RMS and PPMS

- Fenebrutinib has a well-established safety profile due to 13 clinical studies with >1200 patients, thereof 535 patients exposed for >1 year; generally well tolerated, mostly non-serious, mild and self-limiting AEs
- Primary endpoint is composite Confirmed Disability Progression 12 (cCDP12); co-primary endpoint in RMS is ARR
- cCDP12 provides a more thorough approach to disability progression, including EDSS (global assessment scale), 9HPT (hand function) and T25FWT (ambulation ability). cCDP12 assesses upper limb function and may detect disease progression earlier
- Ph III program in RMS and PPMS to start enrollment in 2020

Ph III trial designs

- Ph III RMS (FENhance)
  - Double-blind treatment
  - Patient population: Ages 18-65 years, MS diagnosis
  - Disease duration ≥12 weeks
  - Baseline EDSS ≥3.5 at screening

- Ph III PPMS (FENtrepid)*
  - Double-blind treatment
  - Patient population: Ages 18-65 years, MS diagnosis
  - EDSS score of ≥4.5 at screening

Primary endpoint

- cCDP12
  - 212 weeks after the initial disability progression, confirmation of at least 1 of the following:
    - confirmed disability progression on Expanded Disability Status Scale (EDSS)
    - ≥20% increase from baseline in 9-Hole Peg Test
    - ≥20% increase from baseline in Timed 25-Foot Walk Test

- *First PPMS study against an active comparator

Hauser S. L. et al, ACTRIMS-ECTRIMS 2020; MS=multiple sclerosis; RMS=relapsing MS; PPMS=primary progressive MS; BL=base line; Q12W=every 12 weeks; * Defined as an increase of ≥1 point from a baseline score of ≤5.5, or an increase of ≥0.5 points from a baseline score of >5.5; EDSS=Expanded Disability Status Scale; 9HPT=9-Hole Peg Test; T25FWT=Timed 25-Foot Walk Test; AE=adverse event
<table>
<thead>
<tr>
<th>Hematology franchise</th>
<th>Other oncology</th>
<th>Immunology</th>
<th>Other Oncology</th>
<th>Immunology</th>
<th>Ophthalmology</th>
<th>Neuroscience</th>
<th>Immunology</th>
<th>Infectious diseases</th>
</tr>
</thead>
</table>

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SMA franchise: Evrysdi in type 1/2/3 SMA
Compelling benefit/risk profile in infants, children, adults

SMN2 splicing modifier

FIREFISH part 2 results in type 1 SMA confirm highly competitive profile

- Efficacy in infants, children, adults
- Durably increases SMN protein throughout the CNS and in peripheral tissues
- Consistent safety profile in over 450 risdiplam-treated patients in trials
- First and only at-home treatment

- Positive Ph III (FIREFISH part 2) in older, symptomatic type 1 infants
- Positive Ph III (SUNFISH part 2) the only placebo controlled study in a broad spectrum of type 2/3 patients (age 2-25)
- US approval achieved in Q3 2020; filed in EU, Brazil, Canada, China and 14 further countries

Servait L., et al. AAN 2020. *Performance criterion=5%, exact binomial test. †As measured by CHOP-INTEND. ‡Performance criterion=12%, exact binomial test. §As measured by HINE-2; ‡Risdiplam in collaboration with PTC Therapeutics and the SMA Foundation. FIREFISH part 2 results in type 1 SMA confirm highly competitive profile.
SMA franchise: Evrysdi in type 1/2/3 SMA
Additional data for switching patients and newborns

**Broadest Ph III program in SMA on-going**

- Ph III (JEWELFISH) switching study fully recruited (n=174); Prior treatments were olesoxime (n=74), Spinraza (n=73), Zolgensa (n=14); RG7800 (n=13); JEWELFISH exploratory efficacy to be reported after 1 year of follow-up in 2021
- Ph III (RAINBOWFISH) presymptomatic study enrollment on-going
- Evrysdi has the potential to become the treatment of choice for the majority of SMA patients as our broad clinical trial program covers the broad, real-world spectrum of people living with SMA – including under-served and under-represented patient populations

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Risdiplam in collaboration with PTC Therapeutics and the SMA Foundation; * Estimated 2020 prevalence in US and EU5
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Enspryng in NMOSD

Significantly reduced frequency and severity of relapses

**Anti-IL-6 receptor mAb**

- Recycling mAb with high-affinity to soluble and membrane-bound IL-6R
- Engineered to enable maximal inhibition of IL-6 signalling
- Convenient SC Q4W dosing at home

**Ph III (SAkura) up to 5 year follow-up (AQP4+ patients)**

- Continued risk reduction of relapse for up to 5 years; AQP4+ patients experiencing a 66% risk reduction, and all patients experiencing a 51% risk reduction vs those originally randomized to placebo; treatment associated with a significant reduction in severe relapses vs placebo
- Pooled longer-term data from the SAkura studies show a continued favorable safety profile
- Roche is actively exploring Enspryng in other rare indications where IL-6 is implicated
### Late stage pipeline update

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1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18  19  20  21
AD: Gantenerumab targeting Amyloid β (Aβ)
Strong target engagement and downstream biological impact

**Anti-Aβ mAb**

- Fully human, anti-Aβ mAb (IgG1) with high affinity to aggregated forms of Aβ
- Highest affinity for neurotoxic oligomers and plaques \(^1,^2\)
- SC administration enables flexibility of home administration

**OLE shows robust Aβ removal**

- Gantenerumab lowers Aβ below positivity threshold towards floor levels without plateau; at 3 years 80% of patients were Aβ-negative in OLE studies
- Gantenerumab reduces levels of downstream biomarkers (phosphorylated Tau) and blocks increases of markers of neurodegeneration (NfL) in patients with familial AD (DIAN-TU study)
- Ph III (GRADUATE 1/2) program with optimized exposure by dose (single dosing scheme) and duration (27 months of treatment) on-going; results expected in 2022

**DIAN-TU shows downstream impact**

- CSF Phospho-Tau levels over 4 years
- CSF NfL levels over 4 years

---

**AD: Semorinemab targeting anti-Tau**

**Ph II (TAURIEL) results for semorinemab expected in H2 2020**

- **Anti-Tau mAb**
  - First-in-class humanized Ab
  - Recognizes N-terminal epitope
  - Targets all known isoforms of full length Tau independent of their phosphorylation status

- **Proposed MOA**
  - Anti-Tau Abs potentially block or slow the spread of pathological tau in the brain

- **Ph I (PK/PD) results**
  - No AEs associated with semorinemab in pre-clinical studies; safe and well tolerated in Ph I
  - Robust biomarker development with two tau PET tracers in development
  - Results from blinded portion of Ph II (TAURIEL) in prodromal-to-mild AD expected in H2 2020; primary endpoint includes CDR-SB; secondary endpoints include cognitive tests (ADAS-Cog13, RBANS Total Score) and functional tests (ADCS-ADL, Amsterdam iADL)
  - Second Ph II (LAURIET) in patients with moderate AD on-going

---

Teng E. et al. CTAD 2019; Kerchner et al. CTAD 2017; PD=pharmacodynamics; PK=pharmacokinetics; HV=healthy volunteer; AD=Alzheimer’s disease; ADAS-Cog=Alzheimer’s Disease Assessment Scale–Cognitive subscale; ADCS-ADL=Alzheimer’s Disease Cooperative Study–Activities of Daily Living Inventory; Amsterdam iADL=Amsterdam Instrumental Activities of Daily Living scale; CDR-SB=Clinical Dementia Rating–Sum of Boxes; RBANS=Repeatable Battery for the Assessment of Neuropsychological Status; Semorinemab partnered with AC Immune; PET=positron emission tomography
AD: Gantenerumab brain shuttle (RG 6102)
Vision: Superior target access leading to slowing of AD progression

**MOA: Superior brain access through brain shuttle technology**

1. mAb injected systemically
2. Brain Shuttle mAb construct binds to TfR1
3. The receptor transports the Brain Shuttle mAb across the BBB
4. Brain Shuttle mAb detaches from the BBB receptor to induce therapeutic effect

**Anti-Aβ-TfR1 fusion protein**

- Gantenerumab with a novel transferrin receptor (TfR1) binding Ab moiety to achieve efficient transport over the BBB and target Aβ engagement in the brain
- Technology could also be applied to other CNS disorders
- Preclinical work provides in vitro and in vivo evidence that binding to the TfR1 receptor facilitates transcellular transport across the Blood Brain Barrier (BBB)
- The first brain shuttle mAb entered the clinic in 2019
- Preliminary Ph I PK/PD data are currently under evaluation to determine next steps

1. Niewohner J, et al. Neuron 2014; 81:49–60; BBB=blood brain barrier; IgG=immunoglobulin G; mAb=monoclonal antibody; TfR1=transferrin receptor 1; Aβ=Amyloid β; CNS=central nervous system; PD=pharmacodynamics; PK=pharmacokinetics
# Late stage pipeline update

1. **Hematology franchise**
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   - FL: mosunetuzumab, glofitamab, Polivy
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   - MM: Venclexta
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Tominersen (HTT-ASO) in Huntington’s disease
First drug to reduce toxic mHTT

Antisense RNA

• Antisense drug binds to wtHTT and mHTT sequence leading to RNase H1 mediated degradation of wild-type and mutant HTT mRNA
• Addresses all patients

Ph II update

• Preliminary analysis of 15 month OLE data show sustained lowering of CSF mHTT exceeds or achieves target reduction range of 30-50% (Q4W; Q8W)
• Safe and well tolerated with no dose-limiting toxicities identified and no patients discontinuing
• Ph III (GENERATION HD1) enrollment completed in Q2 2020; results expected in 2022
• Data from the Ph I/II and Ph III OLE studies and the HD Natural History study expected in 2021

Ph III program

2018

OLE Ph II (N=46)

2019

Ph III GENERATION HD1 (N=781)

HD Natural history study (N=100)

2020

OLE Ph III GEN-EXTEND (N=950)

2021

Schobel SA. et al, Cure Huntington’s Disease Initiative - 15th Huntington’s Disease Therapeutics Conference CHDI 2020; mHTT=mutant huntingtin; wtHTT= wild-type huntingtin; CSF= cerebrospinal fluid; OLE=open-label extension; Q4W=every 4 weeks; Q8W=every 2 months; IT=intrathecal; HTT-ASO licensed from IONIS Pharmaceuticals
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Micro-dystrophin Gene Therapy (SRP-9001) in DMD
Positive 1 year safety & efficacy data published in JAMA Neurology

Micro-dystrophin gene therapy

- AAVrh74 vector: low likelihood of pre-existing immunity and high tropism for skeletal & cardiac muscles
- Expression potentiated by the MHCK7 promoter in cardiac & skeletal muscles
- Transgene retains critical elements of dystrophin for a functional protein

Ph I/IIa open-label trial results (n=4)

- 81.2% of muscle fibers expressing micro-dystrophin by immunohistochemistry with a mean intensity of 96% at the sarcolemma at 12-wks; adjusted for fat and fibrotic tissue Western blot showed a mean expression of 95.8%
- All patients showed improvements in NSAA score (mean, 5.5 points up to one year); therapy was well tolerated with minimal adverse events up to one year after treatment
- Planning for two global Ph III trials in ambulatory and non-ambulatory DMD patients are ongoing

Immunofluorescence staining

Western blot

North Star Ambulatory Assessment (NSAA)

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<th>Parameter</th>
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<td>-81.66%</td>
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<tr>
<td></td>
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</tr>
</tbody>
</table>

Mendell J. R. et al, JAMA Neurol. 2020 Jun 15; SRP-8011 partnered with Sarepta; License and collaboration agreement with Sarepta Therapeutics in Duchenne Muscular Dystrophy (DMD), securing exclusive ex-US commercial rights to SRP-9001, their gene therapy for DMD, and the right to opt-in to their broader DMD portfolio outside of the US
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Prasinezumab in Parkinson’s disease (PD)
Primary not met, but encouraging core PD motor signs

**Anti-α-synuclein mAb**
- Humanized mAb designed to target aggregated forms of α-synuclein
- Inhibiting cell-to-cell spreading of pathogenic forms of α-synuclein, resulting in slowing of PD progression

**Ph II (PASADENA part 1) 52 weeks results**
- First Ph II (PASADENA) results were presented at MDS 2020 (poster session); additional results (including digital biomarker data) to be presented at the MDS presentation on Sep 15
- Study did not meet its primary endpoint (MDS UPDRS total score)
- Positive signals of efficacy on multiple pre-specified secondary assessments of motor function including motor signs (MDS UPDRS part III)
- Totality of data is being evaluated to determine next steps

- **Change in MDS UPDRS part III**
  - Pooled: -1.44, 80% CI=[-2.63, -0.26], -25%
  - Low dose: -1.68, 80% CI=[-3.48, -0.27], -34%
  - High dose: -1.02, 80% CI=[-2.64, 0.61], -18%

- **Time to worsening of motor signs (+5pts MDS UPDRS part III)**
  - Pooled: HR 0.82, 80% CI=0.64 to 0.99
  - Low dose: HR 0.77, 80% CI=0.63 to 0.96
  - High dose: HR 0.87, 80% CI=0.70 to 1.07
Prasinezumab in Parkinson’s disease

Digital biomarker active tests supporting clinical development

Novel measurements & digital endpoints

Digital biomarkers - providing enhanced patient insights and novel endpoints

- Clinical trials utilizing mobiles, wearables and gaming devices
- More sensitive, precise and objective
- Continuous and longitudinal measurement captures episodic and rare events
- Reduced assessment burden and greater real-world relevance
Roche Pharma Day 2020

Late Stage Immunology, Ophthalmology & Infectious Disease

Cristin Hubbard | Senior Vice President, Immunology, Infectious Disease & Ophthalmology, Global Product Strategy
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Recombinant human Pentraxin-2 in fibrotic diseases

Evaluating new options to treat fibrosis in multiple diseases

**Recombinant human pentraxin-2 (rhPTX-2)**

- First-in-class rhPTX-2
- PTX-2 is an immune regulatory protein that binds DAMPs with specificity for fibrotic tissue
- Received BTD for IPF

**MOA: PTX-2 inhibits fibrosis formation**

- PTX-2 binds monocytes and macrophages via the FcγR and shifts the balance of monocyte differentiation from pro-fibrotic macrophages, fibrocytes to pro-resolutive macrophages
- Serum PTX-2 levels are reduced in patients with IPF, myelofibrosis and other fibrotic diseases; low PTX-2 levels correlate with increased disease severity
- High unmet medical need remains for further slowing lung function decline on top of SOC

**Fibrotic tissue in IPF**

IPF=interstitial pulmonary fibrosis; PTX-2=pentraxin-2; DAMPs=damage-associated molecular patterns; MOA=mechanism of action; FcγR=Fcy receptor; SOC=standard of care
Recombinant human Pentraxin-2 in IPF
Efficacy as monotherapy or in combination with standard of care

Ph II results in IPF

- rhPTX-2 resulted in a significantly slower decline in lung function over 28 weeks vs placebo (-2.5% vs -4.8%); most patients received parallel treatment with SoC and no unexpected adverse events with combination treatment were noted
- Ph III (STARSCAPE) of rhPTX-2 + SOC (Esbriet or Ofev) in IPF to start in Q4 2020
- Ph II trial in myelofibrosis on-going; first results expected in Q4 2020

Raghu et al; JAMA 2018;319(22):2299-2307; IPF = interstitial pulmonary fibrosis, FVC = forced vital capacity; 6MWD = Six minute walk distance; SoC = standard of care; FPI = first patient in
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Gazyva in B-cell mediated diseases
Potential benefit in B-cell mediated diseases

Gazyva increases B-cell depletion

Type II anti-CD20 region
- Increased direct cell death
- Decreased CDC
- Reduced CD20 internalization

Glycoengineered Fc region
- Higher FcγR affinity
- Increased ADCC/ADCP

- Greater potency than Rituxan in depleting peripheral and tissue B-cells
- Recent studies suggest that tissue based B-cells play a major role in lupus nephritis and a more complete depletion is needed

Evaluating Gazyva in B-cell mediated diseases with high unmet need

- **Autoreactive B cells in LN:**
  - Secrete pathogenic autoantibodies & pro-inflammatory cytokines
  - Present self-antigens
  - Activate T cells

- **Lupus nephritis (Ph III (REGENCY) to start in Q3 2020)**
- **Membranous nephropathy (Ph III expected to start H1 2021)**
- **Potential additional opportunities**
  - Non-renal systemic lupus erythematosus
  - Several other diseases

Moessner et al., Blood, 2010; Niederfellner et al., Blood, 2011; Dalle et al., MCT, 2011; Jak et al., Blood, 2011; Alduaij et al., Blood, 2011; Lim et al., Blood, 2011; Honeychurch et al., Blood, 2012; Pievani et al., Blood, 2011; Bologna et al., JI, 2011; Braza et al., Haematologica, 2011; Patz et al., BJH, 2011; CDC=complement-dependent cytotoxicity; ADCC=antibody-dependent cell-mediated cytotoxicity; ADCP=antibody-dependant cellular phagocytosis; MOA=mechanism of action
Gazyva in lupus nephritis (LN)
Ph III (REGENCY) to start in Q3 2020

**Ph II (NOBILITY) results**

- Complete renal response (CRR)
  - Week 52: 35% Gazyva + MMF, 23% Placebo + MMF
  - Week 76: 40% Gazyva + MMF, 18% Placebo + MMF

- Overall renal response (CRR or PRR)
  - Week 52: 56% Gazyva + MMF, 38% Placebo + MMF
  - Week 76: 51% Gazyva + MMF, 29% Placebo + MMF

**Ph III trial design (REGENCY)**

- Single pivotal Ph III to replicate Ph II (NOBILITY)
- Primary endpoint is complete renal response (CRR); secondary endpoints include partial clinical response (PRR)
- Ph III (REGENCY) to start in Q3 2020

- Ph II (NOBILITY) met both primary and key secondary endpoints with no new safety signals
- BTD for Gazyva in LN awarded by the FDA
- Ph II update (104 weeks) to be presented

Furie R. et al; ACR 2019; MMF=mycophenolate mofetil
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Inflammatory bowel disease (IBD) program on-going
Ph III program of etrolizumab in Crohn’s Disease reading out in 2021

Etrolizumab
- Gut-selective, dual α4β7/αEβ7 anti-integrin antibody
- Development of novel patient-reported outcome measures for UC and Crohn’s disease continues

Ph III

IL-22-Fc fusion protein
- Novel non-immunosuppressive MOA
- Restores and protects gut epithelium
- Ph IIb in UC ongoing; N~270

Ph II

RG6287
- Preserves epithelial cell survival
- Ph I on-going

Ph I

IgG-IL-2 fusion protein
- Promotes regulatory T-cell proliferation
- Ph Ib on-going

Etrolizumab in CD: Ph III (BERGAMOT) interim results

- >70% of patients in cohort 1 were TNF IR, representing a population with high unmet need; symptomatic remission was seen at week 6 and observed through week 14; clinically meaningful endoscopic improvement was demonstrated
- Well tolerated; frequency of adverse events comparable to placebo
- Ph III enrolling with final data expected in 2021

Sandborn et al; UEGW; October 2017; Barcelona, Spain; CD=crohn’s disease; UC=ulcerative colitis; MOA=mechanism of action, TNF IR is defined as patients who are refractory to or intolerant of TNF inhibitors
Late stage pipeline update

1. Hematology franchise
   - DLBCL: Polivy, glofitamab, mosunetuzumab
   - FL: mosunetuzumab, glofitamab, Polivy
   - AML: Venclexta
   - MM: Venclexta
   - MDS: Venclexta

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   - TNBC: Tecentriq, ipatasertib
   - HR+: SERD (RG6171), PI3Kαi (RG6114)
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   - Hemophilia A: Factor VIII Gene Therapy
   - PNH: cromalimab

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Late stage ophthalmology progressing rapidly
**PDS and faricimab with the potential to address key unmet needs**

Opportunity to differentiate on durability and improved efficacy

- Faricimab: potential to improve on efficacy
- Anti-VEGF monotherapies
- Faricimab: Potential to improve on durability of response
- Port Delivery System: reduces real world Tx burden

*For illustrative purposes only*
Port Delivery System (PDS) Platform
New indications and next generation bispecifics (DutaFabs)

Ph III trial design (PAGODA) in DME

- In the US and EU diabetic eye disease (DME, DR) is the leading cause of vision loss in working age adults
- Ph III (PAGODA) results in DME expected in H1 2022
- Ph III (PAVILION) in DR started in Q3 2020

DutaFabs: A new PDS compatible bispecific format

- DutaFabs are a novel bispecific Fab format significantly smaller than traditional full sized bispecific antibodies
- DutaFabs are compatible with the PDS technology, potentially enabling increased durability beyond Q6M
- 3 DutaFabs with novel dual MOAs in development

CI-DME= center-involved diabetic macular edema, DR=diabetic retinopathy; BCVA=best corrected visual acuity; mAb=monoclonal antibody; MOA=mechanism of action
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Faricimab in nAMD
Potential to stabilize retinal vasculature and improve treatment durability

- First bispecific Ab in ophthalmology binding simultaneously to VEGF and Angiopoietin2 (Ang2)
- Ang2 inhibition may improve vascular stability and reduce retinal inflammation

Khanani et al, AAO Subspecialty Day 2018; nAMD=neovascular age-related macular degeneration; VEGF=vascular endothelial growth factor; BCVA=best-corrected visual acuity; *Linear model adjusted for baseline BCVA, previous macular laser treatment status, BCVA category (≥ 64 letters vs ≤ 63 letters)

Ph II (STAIRWAY) results in nAMD

- BCVA gains with faricimab Q16W flexible dose and Q12W comparable with ranibizumab Q4W
- 12 weeks after last loading dose 65% of patients had no disease activity and could potentially benefit from Q16W dosing
- Ph III (TENAYA and LUCERNE) enrollment completed; results expected Q1 2021
Faricimab in DME
Potential for improved efficacy and durability

**Ph II (BOULEVARD) results in DME**

- Robust BCVA efficacy gains with a mean of +13.9 letters from baseline
- Statistically significant gain of +3.6 letters over Lucentis
- Durability shown with median time to disease reactivation of 15.1 weeks for faricimab vs 8.6 weeks for Lucentis

**Ph III trial design (YOSEMITE, RHINE)**

- Primary endpoint: Mean BCVA Δ from baseline at 1yr; arm B to evaluate personalized treatment interval of Q12W or Q16W
- Ph III data expected in Q4 2020
- Ph III in RVO to start in 2021

Sahni et al, Ophthalmology 2019;126:1155-1170; DME=diabetic macular edema; BCVA= best-corrected visual acuity; *Linear model adjusted for baseline BCVA, previous macular laser treatment status, BCVA category (≥ 64 letters vs ≤ 63 letters); RVO= retinal vein occlusion
Roche Pharma Day 2020

_Infectious Diseases: A close look at our HBV pipeline_

_John Young_ | Global Head of Infectious Diseases, pRED
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Hepatitis B: High global unmet need

High burden of disease with life-threatening complications

Hepatitis B Virus (HBV)

- Infection: 257m patients are infected with Hepatitis B, 86m in China
- Treatment: Low cure rates and life-long therapy with current SOC (<0-3% cure rate after 1yr of therapy)
- HCC: 25% of untreated HBV patients will develop hepatocellular carcinoma
- Death: 887k patients die yearly from complications of HBV, 7th leading cause of death worldwide

Reference: WHO July 2018
Hepatitis B surface Antigen (HBsAg) loss is the most important endpoint for functional cure with finite treatment duration

**HBsAg detection**

- Total HBsAg is quantitatively measured by Immunoassay (Elecsys HBsAg II quant II, Roche)

**HBsAg decline associated with significantly improved patient outcomes**

<table>
<thead>
<tr>
<th>Relative Risk</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver decompensation</td>
<td>0.28</td>
<td>0.13</td>
<td>0.59</td>
</tr>
<tr>
<td>HCC</td>
<td>0.30</td>
<td>0.20</td>
<td>0.44</td>
</tr>
<tr>
<td>Transplant/Death</td>
<td>0.22</td>
<td>0.13</td>
<td>0.39</td>
</tr>
<tr>
<td>Composite first clinical event</td>
<td>0.31</td>
<td>0.23</td>
<td>0.43</td>
</tr>
</tbody>
</table>

- Meta-analysis of 28 studies with nearly 190,000 chronic HBV patients
- Clear association between HBsAg seroclearance and improved outcome
- HBsAg seroclearance as primary endpoint in clinical trials supported

Roche HBV strategy

Combining antiviral and immunomodulatory agents

Antiviral agents

- **HBV life cycle**
  - Entry
  - Secretion
  - Encapsulation
  - Reverse Transcription
  - Transcription

- **Nucleos(t)ide**
- **CpAM (Core protein Allosteric Modulator)**

Immunomodulators

- **Virus mediated suppression**
- **Novel Immunomodulator**
  - Peg-IFNα
  - TLR7 Agonist

Functional cure

Standard of Care
HBV siRNA (RG6346)
Inhibiting HBV gene expression by targeting the viral genome

- Proprietary liver-targeted RNAi technology (GalXC™) with unique ‘tetraloop’ folded design
- Designed to inhibit HBV gene expression through targeting of S open reading frame of the HBV genome

Ph I (dose finding) interim results

- Durable HBsAg decline up to day 336
- 6 out of 10 patients, who completed day 112, had HBsAg < 100 IU/mL
- Safe and well tolerated

*Interim analysis from 25 June 2020 data cutoff; https://investors.dicerna.com/static-files/0507fc43-4023-4a40-92fb-0c06b9c4a4b7; In collaboration with Dicerna
CpAM (RG7907)

Leads to incorrect assembly of HBV core protein followed by degradation

Core protein allosteric modulator (CpAM)

- Class I CpAM
- Heteroarylpurimidine derivatives
- Aberrant core protein aggregates that are subsequently degraded
- Functional nucleocapsids

Ph I (dose finding)

- Strong HBV DNA decline in all patients within first week of treatment
- 81% (13/16) HBeAg-negative patients achieved HBV DNA levels below LLOQ (20 IU/ml)

EASL 2019 poster FRI-219; HBeAg=Hepatitis B e-antigen; LLOQ=lower limit of quantification
TLR7 agonist (RG7854)
Stimulating innate and adaptive antiviral response via TLR7 pathway

**TLR7 agonist (RG7854)**

- TLR7 detects single-stranded viral RNA and mediates anti-viral cytokine production and dendritic cell activation
- Unique double pro-drug selectively activated in the liver

**Ph I (dose finding) results**

<table>
<thead>
<tr>
<th>Dose (mg)</th>
<th>ISG15 Fraction responding</th>
<th>ISG15 Geometric mean fold change (range)</th>
<th>OAS1 Fraction responding</th>
<th>OAS1 Geometric mean fold change (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0/16</td>
<td>-</td>
<td>0/16</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>1/8</td>
<td>2.4 (2.4–2.4)</td>
<td>0/8</td>
<td>-</td>
</tr>
<tr>
<td>10</td>
<td>0/0</td>
<td>-</td>
<td>0/8</td>
<td>-</td>
</tr>
<tr>
<td>20</td>
<td>1/0</td>
<td>2.6 (2.9–2.9)</td>
<td>0/8</td>
<td>-</td>
</tr>
<tr>
<td>40</td>
<td>1/0</td>
<td>2.9 (2.9–2.9)</td>
<td>0/8</td>
<td>-</td>
</tr>
<tr>
<td>60</td>
<td>1/0</td>
<td>2.6 (2.6–2.6)</td>
<td>2/8</td>
<td>2.4 (2.0–2.10)</td>
</tr>
<tr>
<td>100</td>
<td>6/8</td>
<td>5.9 (2.3–20.3)</td>
<td>5/8</td>
<td>3.8 (1.9–6.0)</td>
</tr>
<tr>
<td>140</td>
<td>8/0</td>
<td>11.6 (2.3–48.0)</td>
<td>8/8</td>
<td>5.5 (2.2–10.1)</td>
</tr>
<tr>
<td>170</td>
<td>8/8</td>
<td>11.2 (2.5–132.2)</td>
<td>8/8</td>
<td>5.5 (2.0–10.0)</td>
</tr>
</tbody>
</table>

- Dose dependent immunomodulatory activity established
- TLR7 activation induces mRNA expression of interferon-inducible genes (e.g. ISG15, OAS1) first observed at 100 mg dose and plateaued at 170 mg dose

Modified from Ma Z et al. Cell Mol Immunol 2015, 12(3):273-82; Gane E et al. EASL 2018; ISG15=Interferon-stimulated gene 15; OAS1=2′-5′-oligoadenylate synthetase 1
Highly adaptive HBV combination platform
Screening novel drug combinations efficiently

Combination platform trial design

- Nimble and adaptive platform for Ph II screening with shared control arm
- First interim analysis after 12 weeks; second interim analysis after 24 weeks; interim analysis helps inform combos B, C and D
- Opportunity to seamlessly add and terminate different drug combinations
CpAM + TLR7 agonist in HBV
First combination to move into Ph II testing

- Ph II combination trial (n=60) started in Q3 2020
- First 12-week interim analysis planned for Q2 2021
- A 4th HBV program molecule (undisclosed novel immunomodulator) moved into Ph I testing
Roche Pharma Day 2020

Late Stage Immunology, Ophthalmology and Infectious Disease

Cristin Hubbard | Senior Vice President Immunology, Infectious Disease & Ophthalmology, Global Product Strategy
Roche’s response to the pandemic
Commitment every step of the way

<table>
<thead>
<tr>
<th>Diagnostics</th>
<th>Pharma</th>
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</thead>
<tbody>
<tr>
<td>• Research &amp; development for best-in-class solutions</td>
<td>• Innovative therapies with various MOAs</td>
</tr>
<tr>
<td>• Deliver high quality diagnostics with flexible throughput</td>
<td>• World-leading biologics manufacturing capacity</td>
</tr>
<tr>
<td>• Strong local support and partnership</td>
<td>• Strong partnerships with healthcare ecosystems across the globe</td>
</tr>
<tr>
<td>• Holistic disease and patient-oriented approach</td>
<td></td>
</tr>
<tr>
<td>• SARS-CoV-2 PCR, Ab &amp; rapid antigen test</td>
<td>• Xofluza</td>
</tr>
<tr>
<td>• SARS-CoV-2/Influenza A/B differentiation test</td>
<td>• Actemra</td>
</tr>
<tr>
<td>• Other routine and diagnostic tests</td>
<td>• REGN-COV2 nAB cocktail</td>
</tr>
</tbody>
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---

**Legend**
- Oncology / Hematology
- Neuroscience
- Ophthalmology
- Infectious diseases
- Immunology
Xofluza in influenza A/B

Ph III studies «prevention of transmission» and infants on-going

**CAP dependent endonuclease inhibitor**

- First-in-class small molecule inhibiting viral RNA replication; stops viral shedding + reduces viral load significantly faster than the current SOC
- Oral, single-dosing
- Safety similar to placebo
- Activity against Tamiflu-resistant and avian strains (H7N9, H5N1)

**Ph III development**

- Ph III (miniSTONE-1) for infants <1yr; results expected in 2022
- Ph III (CENTERSTONE) for prevention of influenza transmission; results expected 2022
- Xofluza approved for healthy people in 24 countries; Global filings for high-risk patients, pediatrics, post-exposure prophylaxis on-going
- FDA emergency use authorization for the cobas SARS-CoV-2 + Influenza A/B test with a single sample, obtained in Q3 2020

**SARS-CoV-2 & Influenza A/B test for cobas 6800/8800**

- cobas® 6800
  - 1,440 results in 24 hours
- cobas® 8800
  - 4,128 results in 24 hours

---

Actemra in severe COVID-19 associated pneumonia

Ph III COVACTA: Primary and key secondary endpoints not met

- Initially approved in RA and GCA
- Approved for CAR T-cell-induced cytokine release syndrome
- Ph III program (REMDACTA, EMPACTA, MARIPOSA, J-COVACTA) in COVID-19 associated pneumonia on-going*

Ph III (COVACTA) in severe COVID-19 associated pneumonia¹

- Ph III (COVACTA) did not meet its primary endpoint of improved clinical status of patients or key secondary endpoint of reduced mortality at day 28
- Potentially clinically meaningful benefits in time to hospital discharge and duration of ICU stay
- Ph III (REMDACTA) results for Actemra + remdesivir expected in Q4 2020

¹ Rosas I, et al; submitted to NEJM Aug 2020; available on medRxiv Aug 2020; RA = rheumatoid arthritis; GCA=giant cell arteritis; CAR T=chimeric antigen receptor T-cell; ICU=intensive care unit; *Additional studies are ongoing and might expand the findings of COVACTA and address outstanding scientifically and medically relevant questions regarding the risk/benefit profile of tocilizumab in COVID-19 in more narrowly defined patient populations and in conjunction with current treatments
Neutralizing antibodies (nAbs) against SARS-CoV2
Promising for treatment and prophylaxis

REGN-10987
REGN-10933
REGN-10928

Antibodies block the virus’s Spike protein, neutralizing its ability to bind and infect

• Two potent, virus-neutralizing Abs binding non-competitively to the critical receptor-binding domain of the virus’s spike protein
• The virus would need to have multiple simultaneous mutations at multiple genetic sites in order to escape the nAb cocktail, which is an unlikely scenario*

nAb cocktails for treatment & prophylaxis

Currently enrolling trials:
• Ph II/III study in hospitalized COVID-19 patients
• Ph II/III study in non-hospitalized COVID-19 patients
• Ph I multidose study in adult volunteers (pre-exposure)
• Ph III prophylaxis of housemates of infected individuals **
• First results expected in September 2020

* A. Baum et al., Science 10.1126/science.abd0831 (2020); In collaboration with Regeneron; ** In collaboration with NIAID
Doing now what patients need next
Roche Virtual Late Stage Pipeline Event 2020
Appendix
### Lung cancer franchise overview

**Expanding coverage throughout lung cancer**

<table>
<thead>
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<th>NSCLC (Sq)</th>
<th>SCLC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALK</td>
<td>EGFR</td>
<td>ROS</td>
</tr>
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**Neo-/Adj**

- **Stage III**
  - **1L**
    - Alcensaa
    - Tacevra + Avastin
    - Rocyclor
    - Gavreto
  - **2L**
    - IMpower150

**IMpower010** (adjuvant) Tacevra
**IMpower030** (neoadjuvant) Tacevra + platinum-based chemo

**SKYSCRAPER-03** tiragolumab + Tacevra

**IMpower110** Tacevra
**SKYSCRAPER-01** tiragolumab + Tacevra
**IMpower150** Tacevra + Avastin + CP
**IMpower130** Tacevra + CnP
**IMpower132** Tacevra + pemetrexed

**Avastin** + carboplatin and paclitaxel

**OAK, POPLAR, BIRCH** Tacevra

**IMpower131** Tacevra + CnP
**IMpower133** Tacevra + carboplatin + etoposide

**SKYSCRAPER-02** tiragolumab + Tacevra + chemo

Data in 2021

NSq=non-squamous; Sq=squamous

* IMpower132 approved in Japan

Approved
Positive readout
PI3K/AKT is the most frequently altered pathway in cancer

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

HR+ = hormone receptor positive; HNSCC= head and neck squamous cell carcinoma; TNBC = triple negative breast cancer
Doing now what patients need next