Driving innovation & growth

Severin Schwan | CEO Roche Group

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Providing solutions for COVID-19

Continued investment in R&D

Growth opportunities

Outlook
Roche’s contribution battling the pandemic

>1 million hospitalized patients received Roche’s treatments

Overview: not all COVID-19 related developments and health solutions captured; EUA=emergency use authorization; RUO=Research use only; * through GenMark acquisition
Uncertainty on how Delta & Omicron will impact medium-term and evolution of COVID

**Example scenarios and key assumption drivers**

*(not exhaustive)*

**Scenario A: COVID steady state**
- Delta & Omicron drive near-term caution and higher vaccination rates
- Vaccine and/or disease induced immunity only lasts 12-18 months, resulting in a large number of “newly re-susceptible” people as of mid-2022
- New “escape” variants evolving causing additional waves

**Scenario B: Delta/Omicron as last major wave**
- Rapid infection of most of the population (including a high number of asymptomatic infections of vaccinated people)
- Vaccination + disease-induced immunity (hybrid immunity) provides long-lasting protection (4+ years)

*The graph shown is purely conceptional to outline basic trends; Source: Roche GPS Medium-Term Probabilistic Model Simulations*
Roche group: Strong underlying business momentum to continue

**Pharmaceuticals**
- New products with strong momentum; impact from biosimilars to flatten
- Major launches in ophthalmology and hematology
- Extensive late-stage news flow in 2022

**Diagnostics**
- Strong routine testing growth expected
- COVID-19 business expected to slow down with increasing vaccination rates, but newly emerging variants with unknown impact

Growth rates at CER (Constant Exchange Rates)
Strong portfolio rejuvenation and diversification

Pharma HY sales as reported in HY reports; AHR=Avastin, Herceptin, MabThera/Rituxan
Note: HY 2011 – Inflammation/Autoimmune/Transplantation shown as Immunology and Virology shown as Infectious diseases
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Continued investment in R&D

Growth opportunities

Outlook
Roche group: Reallocating resources to strengthen innovation

Continued investments into R&D to drive future growth & medical advances

- Re-allocate resources into R&D while working on and protecting profitability
- All departments of Roche aligned on supporting innovation: transformation ongoing in G&A, M&D, Finance and R&D
- Driving digitalisation throughout the entire Pharma/Diagnostics value chains
# Pharma: Broadest set of technology platforms

<table>
<thead>
<tr>
<th>Small molecules</th>
<th>Bi-specifics</th>
<th>Fusion protein</th>
<th>mAb</th>
<th>Antibody drug conjugate</th>
<th>Neoantigen vaccines</th>
<th>Personalized T cells</th>
<th>Antisense RNA</th>
<th>Gene therapy</th>
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<tbody>
<tr>
<td>Ipatasertib</td>
<td>mosunetuzumab</td>
<td>PD1-IL2v</td>
<td>CD19-4-1BB</td>
<td>Activated T cell with neoantigen specificity</td>
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<td>glofitamab</td>
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<td>FAP-4-1BBL</td>
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<td>Giredestrant</td>
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<td>MAGE-A4</td>
<td>ImmTAC</td>
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<td>KRAS G12C</td>
<td>Her2 x CD3</td>
<td>IL15/IL15Ra-Fc</td>
<td>FAP-CD40</td>
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<td>TLR7 agonist</td>
<td>glypican-3 x CD3</td>
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<td>Belvarafenib</td>
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<tr>
<td>SHP2i</td>
<td>PD1 x TIM3</td>
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<tr>
<td>Target oncogenes, induce apoptosis, suppress tumor growth</td>
<td>PD1 x LAG3</td>
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<td></td>
<td>TVRP1-CD3</td>
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<tr>
<td></td>
<td>Engage and activate T cells to kill tumour cells</td>
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</tbody>
</table>

**Pharma: Broadest set of technology platforms**

- **pd1-IL2v**
- **cd19-4-1BBL**
- **FAP-4-1BBL**
- **MAGE-A4**
- **ImmTAC**
- **IL15/IL15Ra-Fc**
- **FAP-CD40**

**Oncolytic adenovirus**

- **Type 5 adenovirus**
- **rh pentraxin-2**
- **OpRegen**

**Recombinant proteins**

**Stem cell therapy**

**Antisense RNA**

**Gene therapy**

- **AVV Adeno associated virus**
- **factor B aso**
- **HBV siRNA**
- **PDL1 LNA**
- **UBE3A LNA**
- **SPK-8011**
- **SPK-8016**
- **SPK-3006**
- **SPK-7001**
- **SRP-9001**

* List of pipeline molecules shown below is not complete; Molecules in the orange box are developed in Oncology.
Recent deals and partnerships
Accelerate drug discovery and driving personalized healthcare

New agreements focused on

- High disease burden
- Promising targets
- Novel enabling technologies
- Decision support

1 Non-exhaustive and illustrative overview of deals and partnerships signed over recent years
Pharma digital strategic priorities

**Research & development**

*Accelerate and de-risk early-stage assets in research* via automation, modelling and AI technologies, e.g. for:
- Better target selection
- Automated compound profiling and selection
- De novo compound design

*More effective and faster clinical trials in development* via integrating clinical and real-world datasets and AI technologies, e.g. for:
- Improved outcomes and enhanced data quality
- Lower cost and operational efficiency
- Faster time to market for new products

**Production & supply chain**

- *Past*: Blockbuster drugs
  - More standardised and homogenous
  - Lower cost and operational efficiency
- *Present*: Targeted medicines
  - More tailored and adaptive
  - Faster time to market for new products
- *Future*: Individualised treatment
  - More patient-specific and effective
  - Higher cost and operational complexity

**Medicine augmentation**

- *Today*: Digitally-enabled therapeutic decisions
- *Future*: Digitally-enabled behaviour change and Digital biomarkers
Providing solutions for COVID-19

Continued investment in R&D

Growth opportunities

Outlook
6 pivotal adjuvant read-outs expected in 2022
Moving earlier in the treatment schedule

Outcomes by cancer type and stage at diagnosis

- Early detection technologies and increasing screening will allow for earlier treatment
- Early treatment increases cure rates and reduces overall treatment rates

Ph III adjuvant trial program for Tecentriq & Alecensa

1 National Cancer Institute, SEER database, literature review
**Tiragolumab with 9 pivotal trials initiated, 4 readouts in 2022**

**Positive OS data in 1L NSCLC presented**

### Ph II (CITYSCAPE) results:
**Tiragolumab + Tecentriq in 1L PDL1+ NSCLC (n=58)**

- With ~30 months of follow-up, an OS hazard ratio of 0.23 was achieved in the PD-L1 TPS ≥50% subgroup and the median OS was not reached
- Tiragolumab + Tecentriq combination well tolerated

### Ph III trial program for tiragolumab

<table>
<thead>
<tr>
<th>Indication</th>
<th>Ph 1</th>
<th>Ph 2</th>
<th>Ph 3</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>1L NSCLC: PD-L1 high</td>
<td>SKYSCRAPER-01</td>
<td></td>
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<td>2022</td>
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<tr>
<td>1L ES-SCLC</td>
<td>SKYSCRAPER-02</td>
<td></td>
<td></td>
<td>2022</td>
</tr>
<tr>
<td>Stage III unres. NSCLC</td>
<td>SKYSCRAPER-03</td>
<td></td>
<td></td>
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<tr>
<td>Neoadj / Adj NSCLC</td>
<td>SKYSCRAPER-05</td>
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</tr>
<tr>
<td>1L NSq NSCLC</td>
<td>SKYSCRAPER-06</td>
<td></td>
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<tr>
<td>Locally advanced ESCC</td>
<td>SKYSCRAPER-07</td>
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<tr>
<td>1L ESCC</td>
<td>SKYSCRAPER-08</td>
<td></td>
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<td>2022</td>
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<tr>
<td>2L+ PD-L1+ Cervical Cancer</td>
<td>SKYSCRAPER-04</td>
<td></td>
<td></td>
<td>2022</td>
</tr>
<tr>
<td>1L SCCHN</td>
<td>SKYSCRAPER-09</td>
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</table>

- **Build on Tecentriq:** Improve on Tecentriq benefit in SCLC
- **Expand into early disease:** Trials initiated in ESCC and early NSCLC
- **Compete in new indications:** H2H trials in NSCLC vs. durva (St III), pembro + chemo (1L)

Byoung Chul Cho et al. ESMO-IO 2021; SCLC=Small Cell Lung Cancer; NSCLC=Non-Small Cell Lung Cancer; SCCHN=head and neck squamous cell carcinoma; ESCC=esophageal squamous cell carcinoma
**Neuroscience portfolio differentiated on targets and technologies**

*Ph III studies in Alzheimer’s to read out in 2H 2022*

<table>
<thead>
<tr>
<th>Ph I (4 NMEs)</th>
<th>Ph II (7 NMEs)</th>
<th>Ph III (3 NMEs, 1LE)</th>
<th>Launched (3)</th>
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<tbody>
<tr>
<td>RG6091 UBE3A LNA Angelman syndrome</td>
<td>UCB 0107 bepranemab Alzheimer’s</td>
<td>RG1450 prasinezumab Parkinson’s</td>
<td>RG1594 Ocrevus MS</td>
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<tr>
<td>RG7637 undisclosed</td>
<td>RG6102 brain shuttle gantenerumab Alzheimer’s</td>
<td>SRP 9001 microdystrophin gene therapy DMD</td>
<td>RG7916 Enspryng gMG</td>
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<tr>
<td>RG8237 undisclosed</td>
<td>RG7412 crenezumab Alzheimer’s</td>
<td>RG7916 Enspryng gMG</td>
<td>RG7916 Evrysdi SMA type 1/2/3</td>
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<tr>
<td>RG6182 undisclosed</td>
<td>RG7908 ralmitaront Schizophrenia</td>
<td>RG7845 fenebrutinib MS</td>
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- **Ph III (GRADUATE I/II) in Alzheimer’s:**
  - ~1,000 participants in each trial and a trial duration of 27 months
  - Most comprehensive data set to be generated
  - Maximised exposure through optimized titration scheme & single target dose regardless of APOE genotype
  - Gantenerumab demonstrated Aβ plaque reduction (80% of patients below amyloid positivity threshold at 3 years in OLE)
  - SC delivery allows home-administration by caregiver

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NME=new molecular entity; LE=line extension; NMOSD=neuromyelitis optica spectrum disorders; DMD=Duchenne muscular dystrophy; gMG=generalised myasthenia gravis; MS=Multiple sclerosis; SMA=spinal muscular atrophy; OLE=open label extension; Risdiplam is developed in collaboration with PTC therapeutics and the SMA Foundation.
Broadening and deepening the ophthalmology pipeline
Building a global ophthalmology franchise

**Faricimab**
- First Roche intravitreal implant
- Positive readout in nAMD\(^1\)
- Ph III results in DME and DR in 2022, Ph III Q9M extension initiated
- FDA approved Oct 2021

**DutaFabs + PDS**
- New dual MOA: Anti-VEGF/Ang2 bispecific mAb
- Positive Ph III results in DME & nAMD, trials in RVO in US/EU
- Expected US launch in Q1 2022

**Anti-HtrA1 mAb in GA**
- DutaFabs enable creation of a novel bispecific Fab, which are significantly smaller than bispecific antibodies
- Compatible with PDS
- Novel pathway in GA secondary to AMD identified by human genetics
- Ph II for anti-HtrA1 Ab fragment in GA started

**Digital solutions & new technologies**
- Develop digital tools for physicians and patients to improve diagnosis and monitor disease progression
- Further explore gene therapy, RNA therapeutics and stem cell therapy

**Global retina market growing to ~$14b by 2024**

**Improved patient outcome and reduced treatment burden**

\(^1\)Non-inferior and equivalent to monthly Lucentis; \(^2\)Fab is the region of an antibody that binds to antigens; Anti-VEGF=anti-vascular endothelial growth factor; Ang2=angiopoietin-2; DME=diabetic macular edema; mAb=monoclonal antibody; nAMD=neovascular age related macular degeneration; PDS=Port delivery system; DR=diabetic retinopathy; Q9M=every 9 months; GA=geographic atrophy
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Growth opportunities

Outlook
Our replace and extend strategy is progressing well

<table>
<thead>
<tr>
<th>Replace ongoing franchises</th>
<th>Entering new franchises</th>
<th>Strong news flow ahead (data readout)</th>
</tr>
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<tbody>
<tr>
<td>MabThera/Rituxan</td>
<td>Oncology:</td>
<td>tiragolumab (SKY-1) in PDL1-high NSCLC</td>
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<tr>
<td>Gazyva, Venclexta, Polivy,</td>
<td>Tecentriq (mUC, SCLC,</td>
<td></td>
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<tr>
<td>mosunetuzumab, glofitamab</td>
<td>HCC, mM), itipatasertib (mCRPC),</td>
<td>tiragolumab (SKY-2) in 1L ES-SCLC</td>
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<td></td>
<td>giredestrant (HR+ BC)</td>
<td>tiragolumab (SKY-8) in 1L ESCC</td>
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<td>Herceptin</td>
<td>Non-malignant hem:</td>
<td>giredestrant (accelERA) in 2L/3L ER+ mBC</td>
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<td>Perjeta, Kadcyla, Phesgo</td>
<td>Hemlibra, SPK-8011,</td>
<td>crovalimab (COMMODORE) in PNH</td>
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<td>crovalimab (PNH, aHUS)</td>
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<td>Avastin</td>
<td>Neuroscience:</td>
<td>mosunetuzumab in 3L + FL</td>
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<td>Tecentriq, Alecensa,</td>
<td>Ocrevus (RMS, PPMS),</td>
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<tr>
<td>Rozlytrek, tiragolumab</td>
<td>fenebrutinib (RMS, PPMS)</td>
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<td>Enspryng (NMOSD, gMG), Evrysdi (SMA), gantenerumab (AD), SRP-9001 (DMD)</td>
<td>gantenerumab (GRADUATE 1/2) in Alzheimer’s disease</td>
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<tr>
<td>Lucentis</td>
<td>Infectious diseases:</td>
<td>etrolizumab (Bergamot) in Crohn’s disease</td>
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<td>Port delivery system (PDS)</td>
<td>Ronapreve (COVID-19)</td>
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<td>faricimab</td>
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<td>Immunology:</td>
<td>Polivy (POLARIX) in 1L DLBCL</td>
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<td>Xofluza</td>
<td>etrolizumab (CD), Gazyva (LN, MN, SLE)</td>
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<td>Esbriet</td>
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<td>rhPentraxin-2</td>
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mUC=metastatic urothelial carcinoma; SCLC=small cell lung cancer; HCC=hepatocellular carcinoma; mM=metastatic melanoma; mCRPC=metastatic castration resistant prostate cancer; BC=breast cancer; PNH=paroxysmal nocturnal hemoglobinuria; aHUS=atypical hemolytic uremic syndrome; 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; SLE=systemic lupus erythematosus; FL=follicular lymphoma; DLBCL= diffuse large B cell lymphoma; T11;14=diffuse large B cell lymphoma; NSCLC=non-small cell lung cancer; ESCC=esophageal squamous cell carcinoma; DME=diabetic macular edema; IA=interim analysis; SCCHN=squamous cell carcinoma of the head and neck; RCC=renal cell carcinoma; HCC=hepatocellular carcinoma
Positive outlook re-iterated

*The graph shown is purly conceptional to outline basic portfolio trends.*

**Pharma late-stage NMEs and Dia launches**

faricimab, mosunetuzumab, glofitamab, tiragolumab, gantenerumab, giredestrant, crovalimab, fenebrutinib, rhPTX-2, SRP-900, etc.

cobas 6800/8800, cobas 5800, cobas pure, cobas pro (high throughput), cobas Mass Spec, cobas Liat, etc.
Doing now what patients need next