Cell & Gene Strategy

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Global Head of Strategy
Basel, September 3, 2019
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Agenda

1. Strategic context
2. Cell & Gene therapies
3. Pricing & Access
Our Strategy

Focus Novartis as a leading medicines company powered by advanced therapy platforms and data science
Focus: We have focused the company

2013A¹

- Innovative Medicines: 56%
- Alcon: 18%
- Sandoz: 16%
- Vaccines and Diagnostics: 3%
- Consumer Health: 7%

Market cap: $194 bn

Today

- Innovative Medicines: 80%
- Alcon: 20%

Market cap: $217 bn³

¹ Includes Sandoz
³ As of Sep 3, 2019
Focus: Uniquely positioning us with scale and focus

Size
Market cap, $bn

≥ 200$bn

J & J

Merck

Pfizer

Roche

< 200$bn

GSK

Sanofi

NOVARTIS

Lilly

AstraZeneca

Amgen

NovoNordisk

Abbvie

Biogen

Gilead

BMS

Celgene

Rx
AH
OTC
AgChem
VC
Gx
Mtech
Other

Conglomerate < 80% of revenues from Rx

Pure-play ≥ 80% of revenues from Rx

% Rx
Focus: Yet diversified across TAs and platforms

<table>
<thead>
<tr>
<th>Company</th>
<th># of TAs</th>
<th>Top-selling drug, % of total sales</th>
<th>Blockbusters, #</th>
<th>Cell</th>
<th>Gene</th>
<th>RLT</th>
<th>RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NOVARTIS</strong></td>
<td>10</td>
<td>8%</td>
<td>15</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Sanofi</td>
<td>10</td>
<td>10%</td>
<td>4</td>
<td>X</td>
<td></td>
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</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>9</td>
<td>13%</td>
<td>11</td>
<td></td>
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<tr>
<td>Merck</td>
<td>9</td>
<td>19%</td>
<td>5</td>
<td></td>
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<tr>
<td>Pfizer</td>
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<td>12%</td>
<td>8</td>
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<tr>
<td>AbbVie</td>
<td>6</td>
<td>62%</td>
<td>3</td>
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<tr>
<td>Amgen</td>
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<td>22%</td>
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<td>X</td>
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<td></td>
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<tr>
<td>AstraZeneca</td>
<td>6</td>
<td>12%</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lilly</td>
<td>6</td>
<td>16%</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Genentech</td>
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<td>19%</td>
<td>4</td>
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<tr>
<td>Bristol-Myers Squibb</td>
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<td>31%</td>
<td>6</td>
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<tr>
<td>Biogen</td>
<td>2</td>
<td>22%</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gilead</td>
<td>2</td>
<td>64%</td>
<td>4</td>
<td></td>
<td>X</td>
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</tr>
<tr>
<td>Biogen</td>
<td>2</td>
<td>21%</td>
<td>8</td>
<td></td>
<td>X</td>
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</tr>
</tbody>
</table>

1 Only TAs with annual 3rd party sales > $500mn; TA definition as per Evaluate Pharma
Source: Evaluate Pharma May 2019

Presence in advanced therapy platforms

- R&D Media Day Basel, Sep 3, 2019
# Transformative Innovation: Platforms Expand Our Game Board

## Pipeline eNPV

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Oncology</th>
<th>Large Molecules</th>
<th>Small Molecules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novel biomaterials</td>
<td>Ophthalmology</td>
<td>Bispecific antibodies</td>
<td>Targeted protein degradation</td>
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<td>Novel biomaterials</td>
<td>Targeted protein degradation</td>
</tr>
<tr>
<td>Neuroscience</td>
<td>Respiratory</td>
<td>Targeted protein degradation</td>
<td>Transcription factors</td>
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<tr>
<td>Respiratory</td>
<td>Cardio-Renal-Metabolic</td>
<td>Inhaled biologics</td>
<td>Targeted protein degradation</td>
</tr>
</tbody>
</table>

- Large molecules: Novel biomaterials, Bispecific antibodies
- Small molecules: Targeted protein degradation

- Pipeline eNPV: $50bn
- Pipeline eNPV: $38bn

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What is Cell & Gene therapy?

**Ex vivo (= Gene modified cells)**

Gene delivery to cells outside the body

- **Delivery vector, e.g.**
  - Lentivirus
    - Electroporation

- **Payload**
  - DNA
  - Genome editing tool

- **Modify**

- **Remove** (or use allogeneic cells)

- **Cell types**

- **Deliver**

- **Diseases**
  - Cancer
  - Monogenic diseases
  - Infectious diseases
  - Cardiovascular
  - Neurological
  - Ocular
  - Metabolic
  - ... (cont.)

**In vivo**

Direct gene delivery to patient

- **Delivery vector, e.g.**
  - AAV
    - Lipid nanoparticle

- **Local injection**

- **Payload**
  - DNA
  - Genome editing tool

**Dominant current delivery vector:**

- **Lentivirus**

- **AAV**

**Note:** AAV = adeno-associated virus
Source: fda.gov; Genioo analysis

R&D Media Day Basel, Sep 3, 2019
Novartis in C&G

Genvec
- Indication-specific collaboration for:
  - Adenovirus (transient expression only)
  - Hearing loss (immune privileged local injection site)
  - CRISPR/Cas9

UPenn
- Broad collaboration with:
  - Lentivirus + CART (safety & efficacy for ex vivo use)
  - Immuno-oncology (high therapeutic need and greater tolerance of safety risks)

Homology
- Indication-specific collaboration with:
  - AAV-based Homologous Recombination gene editing
  - Sickle cell & Ophtha, in vivo & ex vivo (local use with lower safety risks)
  - Exploratory projects to validate platform

Caribou
- Broad license for CRISPR/Cas9 research use

Intellia
- Indication-specific collaboration with:
  - CRISPR/Cas9
  - Ex vivo cell therapy with CART and HSCs (safest options)

Spark Therapeutics
- EU and ROW license to Luxturna:
  - AAV2 based Ophtha program, in vivo local

Acquisition:
- AAV9 based Neuro programs, in vivo systemic
- GMP manufacturing
- IP/FTO AAV9 in selected indications
Competition: Acquisition puts Novartis in visible pole position in C&G

# of gene therapy deals** by technology type; top 35 pharma companies most active in gene therapy; 2009 – Jun 20th 2018

The field is young – ongoing investment in technology, pipeline, manufacturing will be critical to success

* GSK recently announced potential divestment of gene therapy activities for rare disease
** Research-restricted deals not counted; oncolytic virus deals excluded; double counts if gene editing and vector technology deals were combined
*** Abbvie, AstraZeneca, Amgen, Astellas, Allergan, CSL, Daiichi Sankyo, Eli Lilly, Sun Pharmaceuticals, Takeda

Source: Company websites; Genioo analysis
Clinical: Opportunity to transform the rare disease landscape, and expand beyond

Most C&G trials today in rare diseases...

... But rare disease C&G could have transformative impact for ~2.7M patients

Prevalent population of rare disease indications being tested in active gene therapy clinical trials outside oncology.

Log scale

Non-rare indications

Rare indications

19%
81%

Indications ordered by prevalence

Σ = ~2.7 million potential patients

1. Non-rare indications include foot ulcer, diabetic neuropathy, angina pectoris, severe hearing loss (Novartis), critical limb ischemia, familial hypercholesterolemia, HIV, and Parkinson’s disease.
2. Estimated prevalence of addressable population. Rare disease defined as <400K prevalent patients in US and Europe (US = ~200K cut-off for orphan designation, plus comparable population in EU).

Source: Clinicaltrials.gov as of Dec. 2017; Medical literature, Prevalence Database, Clarivate Analytics; orphanet, raredisease.org, Genioo analysis
Treatment dynamics: Treatment front-loaded for prevalent vs. incident population

![Graph showing treatment dynamics]

- **One-time treatment**
- **Conventional treatment**

- Patients treated, #
- Time

- Year 0
- Year ~4
- Year ~8
Risks: Risks remain for C&G expansion

**Sustainability of rare disease pricing**
- Disproportionate share of drug spend in rare diseases today in critical markets

**Safety risk**
- A single adverse event could slow adoption

**Limited therapeutic expansion**
- Expansion requires solving challenging technical limitations
Problems to solve: Three areas where gene therapy technology innovation would be useful

1. Delivery
   Expanding gene therapy to new indications and TAs

2. Payload

3. Manufacturing
   Improving yields, cycle times, and costs
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What is value-based healthcare?

Value-based healthcare: “linking health costs directly to patient outcomes”

Value = \frac{Outcome}{Cost}

Michael Porter/Elizabeth Olmsted Teisberg, 2006, “Redefining health care: creating value-based competition on results”
Why Novartis is advocating value-based healthcare

**Innovators**
- Develop drugs that create high value
- Need to be rewarded for long-term investments

**Followers**
- Develop «me-too»-drugs
- Are cost-focussed

Support value-based healthcare vs. Oppose outcome focus
One-time therapies challenge us to balance affordability and a more holistic view of value

<table>
<thead>
<tr>
<th>Value Type</th>
<th>Example</th>
<th>Included?</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Value</td>
<td>e.g. survival</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Patient Value</td>
<td>e.g. quality of life</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>System Value</td>
<td>e.g. reduced hospitalizations</td>
<td>✔</td>
<td>Multi-morbidity cost impacts not always fully included</td>
</tr>
<tr>
<td>Societal Value</td>
<td>e.g. productivity</td>
<td>×</td>
<td>No value outside of direct healthcare costs included. HTA methods review critical</td>
</tr>
</tbody>
</table>

Key considerations:

• Balancing cost effectiveness and budget impact
• Balancing uncertainty
Future: In the long run, C&G will be a core platform for innovative medicines

Modular therapeutic tools with more predictable development outcomes and lower cost

“Med-tech” like engineering innovation cycles with faster time to market

Broader therapeutic applications across disease areas

Costs and prices come down closer to biologics
Thank you