Current and future trends in Personalised Healthcare

Bruce Jordan, International Business Leader
Companion Diagnostics (CDx)
Why Personalised Healthcare (PHC)?

PHC is the central pillar to Roche’s strategy

Success stories to date – life-changing improvements

Future examples highlighting Asthma and Alzheimer’s

Summary
PHC is about addressing unmet need
Give patients a treatment that works!

<table>
<thead>
<tr>
<th>Today’s Medical need</th>
<th>Personalised Healthcare</th>
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</thead>
<tbody>
<tr>
<td>Non-responders to current therapy*</td>
<td>The right therapy for the right group of patients</td>
</tr>
<tr>
<td>Cancer 75%</td>
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<tr>
<td>Alzheimer’s 70%</td>
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<tr>
<td>Arthritis 50%</td>
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<tr>
<td>Diabetes 43%</td>
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<tr>
<td>Asthma 40%</td>
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<tr>
<td>Depression 38%</td>
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</table>

1998–2014: 1% of NDAs with CDx+

By 2030: up to 80% of NDAs with CDx#

Need for highly differentiated medicines that positively impact public health

Healthcare Pressures:
Benefit-Risk Ratio

Economic Pressures:
Benefit-Cost Ratio

New Technologies:
Expanded Capabilities

PHC – driver of change
Key to enabling highly differentiated medicines
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Summary
Roche uniquely positioned to drive PHC

Translating excellence in science into effective treatments

→ Combine expertise in molecular biology and technologies to benefit patient
PHC requires collaboration across the value chain. Bringing together the right capabilities at the right time.
PHC at Roche – an integral part of our business
Results of sustained efforts

Research

>350
Internal collaborations on biomarker and/or companion diagnostic programs

Development

8/10
New Phase III molecules have companion diagnostics and/or biomarker program

On-market

5/24
FDA-approved oncology drugs requiring a companion diagnostic
## PHC with 3rd parties - Leading with companion deals

**Roche works with many pharma companies**

<table>
<thead>
<tr>
<th>Company</th>
<th>Deals</th>
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<tbody>
<tr>
<td>Roche</td>
<td>19</td>
</tr>
<tr>
<td>Qiagen</td>
<td>12</td>
</tr>
<tr>
<td>Agilent/Dako</td>
<td>11</td>
</tr>
<tr>
<td>Abbott</td>
<td>9</td>
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<tr>
<td>Myriad Genetics</td>
<td>9</td>
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<tr>
<td>MDx Health</td>
<td>6</td>
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<tr>
<td>Foundation Medicine</td>
<td>5</td>
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<tr>
<td>Danaher</td>
<td>4</td>
</tr>
<tr>
<td>Siemens</td>
<td>4</td>
</tr>
<tr>
<td>BioMerieux</td>
<td>3</td>
</tr>
</tbody>
</table>

Deals since 2009; Source: Axience Analysis of public announcements / press releases
PHC is a strategic choice of Roche
At Roche, PHC is a reality now

“We see an enormous potential and huge opportunities in PHC. Targeted therapies and diagnostic tests that help to improve medical decision-making not only offer clinical benefits for patients but are also attractive through health economic benefits to regulatory authorities and payers.”

“At Roche Personalised Healthcare is a reality now!”

Severin Schwan, CEO Roche
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Summary
Understanding disease mechanisms
New technologies allow better insights and deeper understanding of diseases.

- Observational biology
- Basic biological mechanisms
- Disease mechanisms

Number of plausible targets: 1,000

Timeline:
- Pre-1950s
- 1950/60s
- 1970/80s
- 1990/00s
- Today
Enabling targeted therapies with diagnostic tools

Targeted therapies - approved

**Herceptin, Perjeta, Kadcyla, HER2 tests**
- Breast cancer
- HER2 expression level

**Tarceva (first-line) & EGFR test**
- Non-small cell lung cancer
- EGFR mutations

**Zelboraf & BRAF test**
- Metastatic melanoma
- BRAF mutations

**Pegasys, HBsAg, HBV and HCV tests**
- Hepatitis B and C
- HBV, HCV viral load, genotype

**Antivirals, HIV viral load testing**
- HIV
  - HIV viral load
Evolution of HER2 overexpressing cancer therapy
Targeted therapy enabled by advances in Pathology

Patient selection
Identify patients who will benefit from therapy

Avoid aggressive chemotherapy and unnecessary treatment

Tumour targeting
Combine the specificity of antibodies with the power of chemotherapy

Increased QoL
Decreased number of (S)AE and risk of disease worsening

Chemotherapy

Targeted therapy + chemotherapy

Highly targeted antibody-drug conjugates

*e.g. Anthracyclines*

*Herceptin, Perjeta, Xeloda*

*Kadcyla*

(S)AE: (serious) adverse event; QoL: quality of life.
PHC delivering game-changing improvements
Advanced cancer – progress seen in 2000 - 2010


* average data, in months
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Summary
New treatments to be enabled by diagnostic tests
Improved targeting through diagnostic tools

- **Cobimetinib (MEK Inhib.)** combo Zelboraf
  - met. melanoma
  - BRAF status

- **Alectinib**
  - Non-small cell lung cancer
  - ALK mutation

- **Mericitabine, Danoprevir**
  - Hepatitis C
  - HCV viral load, genotype

- **Human rFSH**
  - Infertility
  - AMH levels

- **Gantenerumab**
  - Alzheimer’s disease
  - Aβ42 levels

- **Lampalizumab**
  - Geographic atrophy
  - Complement factor I

- **Lebrikizumab**
  - Asthma
  - Periostin levels

- **Etrolizumab**
  - Ulcerative colitis
  - Beta 7 integrin subunit

Note: All in development, not commercially available
Asthma – heterogeneous disease
Potential for targeted treatment paradigms in asthma

- **Asthma**
  - 235 million asthma patients worldwide, and more than 200,000 deaths per year
  - Asthma complex disease with marked heterogeneity
  - Over-expression of IL13 is a critical mediator of airway inflammation\(^1\)
  - Different mechanisms lead to symptoms clinically called ‘asthma’
  - Patients move up/down treatment steps (ICS/OCS) until control is achieved and maintained
  - Asthma treatment so far has been a one-size-fits-most approach

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IL-13 is a significant player in severe asthma

Periostin is a surrogate blood biomarker for high lung IL-13

- The periostin gene, together with CLCA1 and serpinB2, were found to be co-upregulated with IL-13 in epithelial cells of subjects with asthma
- Only Periostin was detectable in blood
- Periostin is known to play a role in eosinophil recruitment, subepithelial fibrosis, and mucus production

Lebrikizumab (aIL-13) Phase II study data
Improvement in lung function greater in periostin high

Mean change at Week 12
Lebrikizumab 14.0%, placebo 5.8% (p=0.03)
Difference 8.2%
180 ml

Mean change at Week 12
Lebrikizumab 5.1%, placebo 3.5% (p=0.61)
Difference 1.6%
30 ml

Error bars correspond to mean ± 1 SD

In Development. Not commercially available
Moving towards greater biomarker driven care in asthma

- In 2 phase IIb studies, Lebrikizumab* significantly improved lung function in severe asthma patients+

- Periostin is a potential biomarker to identify patients more likely to benefit from lebrikizumab*+

- A periostin immunoassay development was initiated in time to enable its use in phase III studies

Lebrikizumab *+ Cobas® Periostin immunoassay* = Identify most likely responders

*In development, not available in the USA

Alzheimer’s Disease is a complex and debilitating disease. Current diagnoses and therapies are very limited.

The field is desperate for advancements to alleviate the heavy burden on patients, caregivers, and healthcare systems.

2013 48 million people

2030 76 million people

2050 130 million people

Early treatment is the key to fighting the disease
Current treatments address symptoms and not disease

<table>
<thead>
<tr>
<th>Brain structure</th>
<th>Normal</th>
<th>First lesions</th>
<th>Major lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Preclinical AD</td>
<td>Prodromal AD</td>
<td>AD dementia</td>
</tr>
<tr>
<td>Time$^1$</td>
<td>&gt;10 years</td>
<td>~5-7 yrs</td>
<td>~7-10 yrs</td>
</tr>
</tbody>
</table>

1. Adapted from Herbert LE et al. Arch Neurol 2003, preventAD.com; Average duration per disease stage:
   >10 yrs pre-clinical, 5-7 yrs pAD, 2-4 yrs mild, 2-4 yrs moderate, 3-4 yrs severe 2. Mueller SG et al. Alzheimers Dement. 2005
PHC is the future of medicine
What is today exceptional will be routine in 2030

Estimated that up to 80% new drugs will come with a CDx in the 2030

<table>
<thead>
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<th>Tx in late clinical development</th>
<th>New Tx</th>
<th>Old Tx</th>
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<tbody>
<tr>
<td></td>
<td>30%</td>
<td>50%</td>
</tr>
<tr>
<td>2014</td>
<td>60%</td>
<td>20%</td>
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<tr>
<td>2020</td>
<td></td>
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<tr>
<td>2024</td>
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<tr>
<td>2030</td>
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% of Therapies (Tx) with CDx

Shift from Oncology to other Disease Areas create more opportunities for RPD

Current Dx CDx market

Late stage drug dev (CT Phase II/III)

Early stage drug dev today (discovery / Phase I)

Personalized Medicine by the Numbers (http://www.personalizedmedicinecoalition.org/)
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• There is a significant unmet need to improve treatment response rates

• Roche addresses this by making PHC central to the strategy of the company

• PHC has the potential to significantly improve delivery of healthcare, bringing benefits to patients, and society

• There are exciting developments that will hopefully bring advancements to patients in many new areas of medicine
Doing now what patients need next