Future Outlook for Companion Diagnostics – Challenges and Chances

Bruce Jordan, VP - International Business Leader CDx Centralised and Point of Care Diagnostics, Roche
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<th>Why Personalised Healthcare (PHC)?</th>
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Personalised Healthcare (PHC) is about addressing unmet need
Give patients a drug that works!

Today’s Medical need
Non-responders to current therapy*

- **Cancer**: 75%
- **Alzheimer’s**: 70%
- **Arthritis**: 50%
- **Diabetes**: 43%
- **Asthma**: 40%
- **Depression**: 38%

Personalised Healthcare
The right therapy for the right group of patients

* Clinical Trends in Molecular Medicine,” Volume 7, Issue 5, 1 May 2001, pages 201-204
Roche uniquely positioned to drive PHC
Translating excellence in science into effective treatments for patients

Combining unique expertise in biology and technologies to benefit patients
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
Scenarios for diagnostic hypotheses

Biomarkers

Predictive biomarkers

Diagnostic Assay

Companion Diagnostic

Selection Claim

Complementary Diagnostic

Predictive Claim
PHC is the future of medicine
What is today exceptional will be routine by 2030

3x more drugs will come with a CDx in the next 15 yrs

Shift from Oncology to other DAs create more opportunities in PHC

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/)
## Agenda

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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

**Aggressive 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

Source: Prof. Ch. Zielinski, University Vienna, Austria, March 2010, "Ergebnisoptimierung in der Therapie maligner Erkrankungen durch moderne Behandlungsstrategien: Einfluss auf die Überlebensdauer von PatientInnen mit Krebserkrankungen", http://www.onkologie-wien.at/forschung-und-lehre/positionspapier/; * average data, in months
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New treatments to be enabled by diagnostic tests
The lab’s increasing role in patient management

Cobimetinib (MEK Inhib.) combo Zelboraf
Metastatic 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
- 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

**High-periostin subgroup**

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

**Low-periostin subgroup**

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

Investor Update

Basel, 29 February 2016

Roche provides update on two identical phase III studies of lebrikizumab in people with severe asthma

♦ One study met its primary endpoint, showing lebrikizumab significantly reduced exacerbations in people with severe asthma; the second study did not meet this primary endpoint

♦ Roche continues to evaluate these study data to better understand the results

♦ Clinical studies in asthma, COPD, atopic dermatitis and idiopathic pulmonary fibrosis are ongoing

In Development. Not commercially available
**Alzheimer’s Disease is a complex and debilitating**

*Current diagnoses and therapies are very limited*

2013  **48** million people

2030  **76** million people

2050  **130** million people


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

Early treatment is the key to fighting the disease

Current treatments address symptoms and not disease

<table>
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<th>Brain structure</th>
<th>Normal</th>
<th>First lesions</th>
<th>Major lesions</th>
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<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>
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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
### Continuously pushing the boundaries

**Focused investment improving patient outcomes & lab efficiency**

#### Testing efficiency

- **Automation**
  - tailored to throughput and specialized needs
- **Workflow**
  - Connectivity beyond Serum Work Area, e.g. Molecular Diagnostics
- **IT-solutions**
  - providing flexibility and mobility
- **Specialty testing**
  - extension of coverage

#### Medical value and test menu extension

#### Main focus areas

- Cardiology
- Infectology
- Oncology
- Women’s Health
- Point-of-Care
Roche LabSol concept
Enabling integration of new PHC technologies

Clinical Laboratory

Serum Work Area

Immunoassays
Clinical Chemistry

Workflow

IT

PoC Hospital
Haematology

Molecular solutions
Perspective from IVD manufacturer’s side

Challenges

- High risk projects
- Small testing volume / niche applications
- Technology-based reimbursement
- Continuously changing Pharma strategy and timelines
- Changing regulatory environment

Chances

- Access to novel biomarkers that may eventually become novel IVD product → differentiated menu
- Additional utility through claim extensions to existing assays
- Leverage clinician outreach of pharma partner
- Multiple partners for same assay

Identifying ways of making the collaboration a win-win is critical
Summary

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

The Clinical Laboratory will play an ever increasing role in patient management decisions

Roche is developing new tests that improve outcomes and that can be integrated into the routine lab setup
Doing now what patients need next