Diagnostics and Personalised Healthcare

Daniel O’Day | Chief Operating Officer
Roche Diagnostics

Roche Diagnostics: Uniquely Positioned

Revaluing in vitro Diagnostics

Driving Personalised Healthcare
Roche Diagnostics
Leader in a growing market

Number 1 in IVD...

... a large and growing market

IVD = in vitro diagnostics
Source: Boston Biomedical Consultants, Company reports, Roche analysis

Strong presence and broad portfolio
Solid basis for future growth

Present in all customer segments

Broad array of technologies

Increasing # innovative products

Source: Roche analysis
Roche Diagnostics: Uniquely Positioned

**Revaluing in vitro Diagnostics**

**Driving Personalised Healthcare**

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**Medical breakthroughs and market demographics**

*Increasing the importance of Diagnostics*

Unmet medical need, Market demographics

Advances in science enabling new insights

Need for personalised healthcare

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**Opportunity to revalue Diagnostics**

IVD < 2% total worldwide healthcare spend
Influences > 60% of critical decision making

European Diagnostic Manufacturers Association (EDMA) 2009
Creating medical value
*Beyond diagnosis … to Personalised Healthcare*

**Diagnostics**
- Screening
- Diagnosis
- Prognosis
- Prediction
- Monitoring

**Companion Diagnostics**
- Treatment selection
- Response prediction
- Treatment monitoring

**Medical value requires new capabilities**
*Roche uniquely positioned to capture the value*

**IVD System Development**
- Reagent kits
- Hardware
- Software
- Technical validation

**Content Development**
- In-house research
- Roche Pharma
- External research

**Clinical Validation**
- Demonstrate clinical utility
- Health economic data
- Regulatory submission

**Clinical Adoption**
- Medical guidelines
- Reimbursement/Premium pricing
- Market uptake via clinicians

Increasing barriers to entry
Roche’s distinctiveness

Significant advantages to both businesses

- biomarkers
- tools & technologies
- validated assays
- regulatory expertise
- commercial reach

Diagnostics

Medical value products

Pharma

Efficient & safe medicines

- new content
- patient samples
- clinical trials
- testing demand
- platform adoption

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Revaluing in vitro Diagnostics

Driving Personalised Healthcare
Creating medical value
Through new diagnostics tests…

**Medical Value**

### Diagnostics
- Screening
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**Cervical Cancer: HPV screening algorithms**
*Growth and market size driven by adoption of screening*

<table>
<thead>
<tr>
<th>Clinical Applications</th>
<th>Number of HPV tests in the US</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ASCUS Triage</strong></td>
<td>~1 m</td>
</tr>
<tr>
<td>Pap → HPV → Colposcopy</td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td></td>
</tr>
<tr>
<td><strong>Adjunct screening</strong></td>
<td>~28 m</td>
</tr>
<tr>
<td>Pap/HPV → Colposcopy</td>
<td></td>
</tr>
<tr>
<td>1 year / 3 years</td>
<td></td>
</tr>
<tr>
<td><strong>Primary screening</strong></td>
<td>~50 m</td>
</tr>
<tr>
<td>HPV → Pap → Colposcopy</td>
<td></td>
</tr>
<tr>
<td>3 years</td>
<td></td>
</tr>
</tbody>
</table>

*U.S. Market: $250 m, 20% growth per year*

Company reports, Roche analysis
**ATHENA Trial demonstrates medical value of HPV testing and Genotyping in Cervical Cancer screening**

- **ATHENA trial** demonstrates medical value of HPV testing and Genotyping in Cervical Cancer screening

  - Targets ASCUS triage, adjunct screening and HPV 16/18 claims
  - Study results confirm variability of cytology and support improved consistency of HPV DNA based cervical cancer screening programs
  - Data support HPV 16/18 genotyping as actionable information for intervention
  - FDA submission mid 2010; data to be presented at IPV, Montreal 07/2010

### The ATHENA Trial

- **Enrolment Completed**

- **Follow-Up**
  - Year 1: 2009 - 2010
  - Year 2: 2010 - 2011
  - Year 3: 2011 - 2012

### Cytology vs. HPV Testing*

<table>
<thead>
<tr>
<th>Site</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology Abnormal</td>
<td>3.7%</td>
<td>5.2%</td>
<td>8.7%</td>
<td>8.8%</td>
</tr>
<tr>
<td>CIN 2+ overall</td>
<td>6.5%</td>
<td>6.1%</td>
<td>5.7%</td>
<td>4.5%</td>
</tr>
<tr>
<td>HR HPV Positive</td>
<td>13.8%</td>
<td>15.7%</td>
<td>15.0%</td>
<td>15.9%</td>
</tr>
</tbody>
</table>

### Immediate follow up for HPV 16/18

<table>
<thead>
<tr>
<th>Deferred follow up</th>
<th>Yearly follow up</th>
<th>Immediate follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCUS HPV+</td>
<td>ASCUS HPV+</td>
<td>2% Increasing risk of CIN2+</td>
</tr>
<tr>
<td>Pap+/HPV-</td>
<td>Pap+/HPV+</td>
<td></td>
</tr>
<tr>
<td>Pap-/ HPV+</td>
<td>Pap-/ HPV-</td>
<td></td>
</tr>
<tr>
<td>Pap-/ HPV-</td>
<td>Pap-/ HPV-</td>
<td></td>
</tr>
</tbody>
</table>

* Wright, TC., EUROGIN 2010

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**Preeclampsia: A significant unmet clinical need**

*PIGF and sFlt1 - first IVD tests for Preeclampsia*

- **Preeclampsia**
  - Leading cause of fetal and maternal death
  - Until recently, no specific tests available
  - Roche developed first automated test to diagnose women with preeclampsia by measuring PIGF and sFlt levels
  - Early detection of patients at risk allows closer prenatal monitoring, early diagnosis and timely intervention

- Occurs in 3%-7% of pregnancies
- Responsible for 18% of all maternal deaths in US
- Costs more than $7 bn in healthcare annually in US

sFlt-1 = soluble fms-like tyrosine kinase; PIGF = placental growth factor

1 World Health Organisation 2 available ex-US

Verlohren et al., Am J of Obstetrics and Gynecology, 2010
Prostate Cancer: Rearrangements between TMPRSS2 and ERG genes found in ~50% of prostate cancer patients

Overall survival from Prostate cancer*

Rearrangement status may determine clinical outcome

- How aggressive is my cancer?
- What should the course of my primary therapy be?
- What is my risk of metastasis?

* Oncogene (2008) 27, 253-263

TMPRSS2= transmembrane protease, serine 2 (androgen responsive gene)
ERG=Ets Related Gene

Assay in development for ERG gene rearrangements
Identifying prostate cancer aggressiveness for appropriate treatment

Patient tumor needle biopsy

Ventana SYMPHONY
Prostate cancer diagnosis via H&E

Imaged Slide Review for Pathologist

Normal
Likely Indolent

3’ Insertion
Likely Aggressive

5’ Deletion
Likely Aggressive

5’ Deletion and 3’ Duplication
Highly Aggressive
Creating medical value
Through Companion Diagnostics…

**Medical Value**

- Screening
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**Companion Diagnostics**

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**Strong pipeline of companion diagnostics**

*Joint Pharma and Diagnostics programs - Oncology*

Roche Pharma targeting multiple pathways

<table>
<thead>
<tr>
<th>Pipeline Drug</th>
<th>Biomarker</th>
<th>Pipeline Assay</th>
</tr>
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<tbody>
<tr>
<td>RG7204 BRAF Inh/PLX4032</td>
<td>BRAF</td>
<td>cobas 4800 BRAF V600E test</td>
</tr>
<tr>
<td>RG7167 MEK Inh/CIF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RG7112 MDM2 Antagonist</td>
<td>p53</td>
<td>AmpliChip p53 array</td>
</tr>
<tr>
<td>RG7112 MDM2 Antagonist</td>
<td>MDM2</td>
<td>cobas MDM2 expression assay</td>
</tr>
<tr>
<td>Tarceva</td>
<td>EGFR</td>
<td>TheraScreen EGFR mutation test</td>
</tr>
<tr>
<td>RG7167 MEK Inh/CIF</td>
<td>KRAS</td>
<td>TheraScreen KRAS mutation test</td>
</tr>
<tr>
<td>RG1273 Pertuzumab N03652 T-DM1</td>
<td>Her1, 2, 3 AREG, BTC</td>
<td>cobas 4800 HER Family expression assay</td>
</tr>
<tr>
<td>RG7521 PDK Inh</td>
<td>PIK3CA</td>
<td>PCR PIK3CA mutations</td>
</tr>
<tr>
<td>RG7422 PDK Inh</td>
<td>PIK3CA</td>
<td>FISH PIK3CA copy number assay</td>
</tr>
</tbody>
</table>

*List not exhaustive*
**Mutation in BRAF Kinase**

*Co-development of test and drug in oncology*

- Identifies patients whose tumor DNA carries BRAFV600E mutation
- Increases feasibility of drug clinical development and probability of success
- IVD timelines aligned with RG7204 accelerated development plan → joint launch

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* BRAF gene mutations detected in ~8% of all cancers, over 50% of malignant melanomas

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**AmpliChip p53 and MDM2 Antagonist**

*Identifying patients with non-mutated tumor suppressor protein*

- Parallel development of AmpliChip p53 array
- Identifies patients with wild-type p53 gene
- Essential for RG7112 clinical development

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* approx. 50% human tumors contain p53 mutants
**Serum markers and Lebrikizumab**

*May identify asthma patients most likely to respond*

**Two distinct Asthma sub-groups**

- Need for non-invasive surrogate markers
- Serum Periostin, IgE and CEA - alone or combined - may predict drug response
- Potential to identify sub-population with improved clinical response to lebrikizumab (anti-IL-13)

- Early Roche Diagnostics - gRED collaboration ensures timely availability of assays for trial program
- Enables patient stratification
- Combining multiple biomarkers may improve sensitivity & specificity

**Roche Diagnostics**

*Driving future value for Roche*

- **Uniquely positioned** to revalue Diagnostics through delivery of medical value
- **Strong pipeline** of innovative Diagnostics and Companion Dx tests
- **Combined strengths** of Roche Pharma and Diagnostics to lead Personalised Healthcare