Opportunities and Challenges in the Development of Companion Diagnostics

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Abbott Molecular
Agenda

- Value of Personalized Medicine
  - Herceptin/PathVysion
  - Xalkori/Vysis Alk

- Challenges and Uncertainties
  - Development
  - Regulatory
  - Commercialization
  - Reimbursement

- Elements of a Successful Partnership
Abbott Molecular is a Division of Abbott Laboratories

- Independent Operating division of Abbott
- State-of-the-art molecular diagnostics facility in Des Plaines, Illinois, U.S.A
- 1000+ employees (300+ scientists and engineers)
- $400+ million sales
- Multiple Products: 510K, PMA, CE, SFDA
- Sun-Times Innovation Award
  - PathVysion (2005)
  - m2000/HIV (2007)
- WSJ Technology Innovation Gold Medal
  - T5000®/PLEX-ID (2009)
Abbott Molecular products use a variety of Technology Platforms....

RealTime PCR

Infectious Disease
- NSCLC
- Melanoma
- CRC

FISH

Bladder Cancer
- Breast Cancer
- Chromosome Enumeration
- Genetics
- Hematology
- Oncology
- Solid Tumors

Sequencing Bead Array

Genetics
- Respiratory
- Infectious Disease

Bioidentification

Applied Research
- Bio-preparedness
- Bio-Pharm
- Clinical Research
- Food Safety
- Forensics
- Surveillance Public Health
• **Personalized Medicine:** the ability to **predict** which therapeutic intervention will be the most **efficacious and safe** based on a test.
Current Therapies Result in Poor Efficacy Rates

• Therapeutic Response Rate

<table>
<thead>
<tr>
<th>Disease</th>
<th>Response Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesics (Cox-2)</td>
<td>80%</td>
</tr>
<tr>
<td>Depression (SSRI)</td>
<td>62%</td>
</tr>
<tr>
<td>Asthma</td>
<td>60%</td>
</tr>
<tr>
<td>Cardiac Arrhythmias</td>
<td>60%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>57%</td>
</tr>
<tr>
<td>Migrane (prophylaxis)</td>
<td>50%</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>50%</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>48%</td>
</tr>
<tr>
<td>HCV</td>
<td>47%</td>
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<tr>
<td>Incontinence</td>
<td>40%</td>
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<tr>
<td>Alzheimer’s</td>
<td>30%</td>
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<tr>
<td>Oncology</td>
<td>25%</td>
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</tbody>
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• Lowest response rate in cancer, 25%

Source: Spear et al., Trends Molecular Medicine 2001;7;201-4.
Personalized Medicine Benefits All Key Stakeholders

- **Physicians**: Prescribe the most effective therapeutic for the disease indication
- **Patients**: Receive the optimal treatment in the minimum amount of time
- **Payors**: Allocate treatment resources in a targeted manner to improve the overall cost effectiveness
- **Regulatory Bodies**: Increase safety and efficacy of prescribed drugs and reduce adverse events
- **Pharma Companies**: Increase R&D productivity and improve efficacy claims with CDx test,
- **Diagnostic Companies**: Demonstrate the value of diagnostic test, broaden product portfolio
Herceptin and PathVysion

• Herceptin is a hallmark of personalized medicine for breast cancer patients and PathVysion serves to identify those that have the potential to respond positively

• PathVysion: The first FISH (gene-based) CDx product
  – Market acceptance of CDx requires clinical data, recognition by guidelines and appropriate reimbursement (payment) for the diagnostic
  – Herceptin was approved in 1998 and PathVysion sales grew mainly as a result of early clinical data
**Crizotinib: Pathway from Compound Identification to Discovery of ALK Target and Clinical Results**

**Crizotinib (PF-02341066) scientific breakthrough:**
Targeting the ALK fusion gene, a direct driver of oncogenesis

<table>
<thead>
<tr>
<th>Lead compound identified</th>
<th>Clinical testing begins</th>
<th>Discovery of EML4-ALK fusion gene</th>
<th>First clinical responses in ALK+ tumors</th>
<th>Phase 2 NSCLC trial initiated</th>
<th>Phase 3 NSCLC trial initiated</th>
<th>ASCO plenary of expanded ALK+ cohort</th>
<th>NEJM publication of ALK+ cohort</th>
<th>FDA approval and Japan filing</th>
<th>Other tumor types investigated</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>2006</td>
<td>2007</td>
<td>2008</td>
<td>2009</td>
<td>2010</td>
<td>2011</td>
<td>2012</td>
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</tbody>
</table>

Rapid timeline from compound identification, target discovery and clinical results

**Clinical results to date:**

- Objective response rate = 61%³
- Disease control rate (CR+PR+SD) = 79% at 8 weeks³
- Median duration of response = 48 weeks³
- Median PFS = 10 months³

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Challenges and Uncertainties—CDx Development

- Development
  - Biomarker selection and establishment of clinical utility
  - Selection of diagnostic methodology
  - Concordance with LDT’s and other methods used in early phases of therapeutic development
  - Dx/Rx trial timeline coordination
  - Specimen availability/informed consent
  - Geographically diverse patient cohorts
Challenges and Uncertainties—Regulatory Approval

- Criteria that define risk for diagnostic tests
  - In the US, companion diagnostic tests require a PMA

- Standards for study design and product performance
  - What is sufficient compelling evidence?
  - What is appropriate correlation with LDT?
  - How can additional tests be launched once the initial clinical utility has been established?

- Coordination of submission and review process

- Coordination of requirements between FDA and other worldwide regulatory agencies

- Criteria and procedures for incorporating diagnostic in therapeutic product labeling
Challenges and Uncertainties—Commercialization

• CDx development has a higher risk profile than most diagnostic product investments

• Commercial strategy must be tailored to fit the scope and breadth of the opportunity

• Global coordination of efforts is key to overall success

• Extensive commercial investment required after the initial product launch
Challenges and Uncertainties—Commercialization

- Regulatory approval is no guarantee of coverage
- Lengthy process to establish coding, coverage and reimbursement
- Insurers are demanding more evidence in setting payment policy
- Insurance company goal is to reduce the cost burden
- Market development and adoption can be difficult and lengthy
- Budget impact, cost effectiveness, HEOR models may be required for drug-test combinations to ensure market access
Key Elements of a Strong Pharma-Diagnostic Partnership

- **Must have Business Incentives for Both Partners**
  - If small Dx revenue stream projected, Risk & ROI may not be sufficient enough for Dx company with traditional model. Pharma support may be needed.
  - Agree on success criteria early, consider performance-based incentives
  - Agreements must address how scope changes will be handled

- **Management and Flexibility**
  - Employ strong project management leadership to drive the project through the calm and stormy seas
  - Establish mechanisms for open communication

- **Leverage Core Competencies**
  - Pharma knows their market access and regulatory process
  - Diagnostic knows their market access and regulatory process
  - Identify interdependencies
  - Each partner must feel confident and trust the other will deliver
Thank you