Delivering Value Through Personalized Medicine: An Industry Perspective

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What is Personalized Medicine?

- Tailoring of medical treatment to the individual characteristics of each patient
- Ability to classify individuals into subpopulations based on susceptibility to a disease or response to a treatment
- Preventive or therapeutic interventions are concentrated on those who will benefit, sparing expense and side effects for those who will not

*Priorities for Personalized Medicine. The President’s Council of Advisors on Science and Technology. September, 2008.*
What Are We Trying to Accomplish?

Delivering the right treatment, to the right patient, at the right time

Right Drug

Drug targeted to specific oncogene or aberrant pathway driving the specific cancer

Right Patient

Patient identified through molecular profiling

Improved Outcomes

Significant improvement in patient outcomes
The Impact of Personalized Medicine

**Benefit to Clinical Development**
- Bigger Treatment Effect
- More Efficient Trial Design + Improved Efficacy of Medicines Developed ➔ Smaller, more efficient Ph 3 Trials

**Benefit to Patients**
- Patients Treated More Likely to Benefit
- More Dramatic Effect in Treated Patients ➔ Clear Value of Treatment

**Graphs**
- Left graph: Unselected Patients vs. Selected Patients
- Right graph: Months on Treatment vs. # Patients
  - 18 Months: 400 Patients
  - 30 Months: 800 Patients
## Everyone Benefits

<table>
<thead>
<tr>
<th>Industry</th>
<th>Regulatory Agencies</th>
<th>Four Ps</th>
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</table>
| **Pharmaceutical Manufacturer**   | - With narrower, better defined patient populations, there may be an enhanced ability to protect patient’s health, ensure safety, quality and efficacy of health products
- Increased productive and efficient drug development | **Patients**
- Provides directed care with optimal therapies
- Receive most appropriate therapy early in their disease process |
| **Diagnostic Developer**          | - More specific information about medicines to help balance the benefit risk profile
- Increased assurance that patients most likely to benefit from a treatment will be those to receive it | **Payors**
- Provides clear evidence for which to base reimbursement decisions
- Avoids unnecessary costs |
|                                   | - Increased opportunity to innovate
- Greater acceptance and use of diagnostic testing within medical community | **Physicians**
- Enables the prescribing of therapies to pts most likely to benefit
- Reduces trial-and-error prescribing |
|                                   | **Policymakers**
- Increased ability to formulate policy to benefit specific populations |
Our Personalized Medicine Approach

• Scientific research and clinical development have **advanced significantly in recent decades**; we now have a deeper understanding of several diseases at a far deeper biological and molecular level.....
  
  • **30 years ago**, lung cancer was divided into small-cell and non-small cell cancer
  
  • **Today**, we understand it to be a group of heterogeneous diseases with different molecular origins
  
  • Pfizer has recognized the potential of this **new way of thinking**—our R&D efforts now focus on:
    
    • Identifying molecules that block genetic biomarkers driving certain diseases—**and shifting focus from a one-size-fits-all approach**
    
    • Delivering medicines and vaccines in a more tailored and targeted approach

Our Goal

To develop therapies with greater safety and efficacy that will be approved for smaller, well-defined patient populations and will ultimately impact disease and improve patient outcomes
XALKORI: Timeline from Compound Identification, Target Discovery and Clinical Results

1994

NPM-ALK fusion discovered in ALCL

2005

Crizotinib identified

STUDY 1001: First in Patient

2006

EML4-ALK fusion discovered in NSCLC

2007

Pfizer Modifies Trial; Works with Abbott to Identify ALK+ Tumors

2008

Partial responses: ALK+ NSCLC

2009

Crizotinib approved by the U.S. FDA (August 2011)

2010

Crizotinib granted priority review by the U.S. FDA (May 2011)


Evidence Development within a New Drug Development Paradigm for Payors and Other Stakeholders

• Understanding the unmet need
  – Molecular epidemiology studies, chart reviews, natural history studies, case studies

• Ability to deal with unique trial designs
  – Single-arm, open-label
  – Cross-over, stacked therapy,
  – Adaptive designs

• Shortened development cycles
  – Availability of Tx prior to ph3 completion
  – Fewer patients exposed, limited data elements and endpoints for approval and reimbursement submissions

• Applying companion diagnostics
  – Consideration for cost of screening and pt. identification
  – Addition of new testing platforms - multiplexing or multiple marker tests

\[ HR = 1.42, \ p=0.18 \]

\[ \text{ALK Positive (n=23)} \]
\[ \text{WT/WT Control (n=125)} \]

Retrospective analysis of never-smokers with lung adenocarcinoma of all stages

Retrospective case-matched survival analysis of ALK-positive patients who did not receive crizotinib


Shaw A et al., Lancet Oncology, Oct. 2011; 12 (11), 1004–1012
XALKORI: Example of Personalized Medicine in Action

• **Efficient Development**
  – Time from discovery to approval exemplifies Pfizer's new approach and commitment to drug development
  – FDA’s approval of Xalkori marks the first new lung cancer drug approval in 6 years

• **Well Defined Patient Population with Improved Efficacy**
  – 3%-5% of advanced NSCLC patients who test positive for the anaplastic lymphoma kinase (ALK) re-arrangement are eligible to receive therapy
  – ALK+ NSCLC patients who were treated with XALKORI had significantly improved PFS compared to SOC therapy

• **Efficient Healthcare Spending**
  – Unnecessary costs may be avoided as therapy is prescribed only to selected patients more likely to respond

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1 PROFILE 1007 Phase 3 study top line report, Pfizer Press Release, June 19, 2012
Still Work to Do: An Evolving Process

• How best to gather a substantial body of evidence to satisfy regulators and payors?

• Incorporation of molecular profiling into “usual” care of cancer patients

• Synchronization of the timing between:
  – Drug development
  – Biomarker discovery
  – Development of companion diagnostic

• Future diagnostic practice: single tests vs. multiple marker tests for specific cancers
How Far Have We Come in 40 Years Since the Declaration of the “War on Cancer”?  

<table>
<thead>
<tr>
<th>Then</th>
<th>Now</th>
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<tbody>
<tr>
<td><strong>Understanding of Cancer</strong></td>
<td></td>
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<tr>
<td>Tumor-focused; uncontrolled cell proliferation</td>
<td>Genetic disease</td>
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<tr>
<td><strong>Detection &amp; Prevention</strong></td>
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<tr>
<td>Physical examination; limited understanding of the importance of early detection</td>
<td>Sophisticated screening and greater understanding of the disease entity; Increasing use of molecular testing</td>
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<tr>
<td><strong>Treatment Options</strong></td>
<td></td>
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<tr>
<td>Surgery, radiation, chemotherapy</td>
<td>Targeted therapies</td>
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As Science Advances, Oncology Drug Development Accelerates

TARGET AND YEAR OF APPROVED TREATMENT

Adapted from Gerber and Minna Cancer Cell: 18: 548, 2010
Pharma & Diagnostic Companies Harness the Potential of Personalized Medicine

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<tr>
<th>Early Development</th>
<th>Ph3</th>
<th>Registration/Launch</th>
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<tr>
<td>- Genomics data drives decision making</td>
<td>- Validated assay</td>
<td>- Define label requirements for CDx</td>
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<tr>
<td>- DX assay, protocol, patient selection tools</td>
<td>- Proof of concept trial design with CDx</td>
<td>- Commercialization strategy</td>
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<tr>
<td>- IP strategy</td>
<td>- Commercial viability of label</td>
<td>- Engage with medical experts</td>
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<tr>
<td>- Phase I plan to measure marker</td>
<td>- Payor research</td>
<td>- Communications strategy for CDx and therapy</td>
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<tr>
<td>- Proof of mechanism strategy</td>
<td>- Reimbursement and Access Strategy</td>
<td>- Reimbursement submissions</td>
</tr>
<tr>
<td>- Commercially viable CDx concept</td>
<td>- Partner commercialization agreement</td>
<td></td>
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<tr>
<td>- External partner agreement</td>
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Success Depends on an Integrated and Collaborative Process

*CDx = companion diagnostic*
Summary

• Personalized medicine is about delivering the right treatment, to the right patient, at the right time

• Innovation and incremental efficiencies may be facilitated as additional biomarkers are identified, greater synergies and partnerships are established between pharmaceutical and diagnostic developers, and increased numbers of patients are swiftly diagnosed and treated

• There is a need for newer thinking and methodological approaches to the development of supportive regulatory and reimbursement evidence within this new paradigm of drug development

• Personalized Medicine benefits multiple stakeholders and supports the efficient use of healthcare resources by concentrating efforts on patients most likely to benefit and sparing expense and side effects for those who will not

• Alignment of incentives for personalized medicine among all stakeholders is critical to support the highest degree of clinical innovation that will improve health outcomes, health care delivery and ultimately, improve the quality of life of patients