Personalized Medicine:
The Changing Landscape of Healthcare

American Association of Clinical Chemistry Annual Meeting
San Diego, California

July 14th, 2007

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Executive Director
Personalized Medicine Coalition
Learning Objectives

• List the advantages for a personalized medicine approach to healthcare

• Illustrate how personalized medicine impacts therapeutic drug management.

• Understand the regulatory issues of personalized medicine reimbursement

• Explain the role of the Personalized Medicine Coalition as a motivator for change.
Personalized Medicine: What is it?
What is Personalized Medicine?

By using molecular analysis to achieve optimum medical outcomes in the management of a patient’s disease or disease predisposition, personalized medicine promises to introduce a new standard of healthcare.
Advocates of personalized medicine stress its potential to:

- Detect disease at an earlier stage, when it is easier to treat effectively
- Enable the selection of optimal therapy and reduce trial-and-error prescribing
- Reduce adverse drug reactions
- Increase patient compliance with therapy
- Improve the selection of targets for drug discovery
- Reduce the time, cost, and failure rate of clinical trials
- Revive drugs that failed clinical trials or were withdrawn from the market
- Avoid withdrawal of marketed drugs
- Shift the emphasis in medicine from reaction to prevention
- Reduce the overall cost of healthcare
What is Personalized Medicine?

Current Practice

One size fits all

Trial and error

Personalized Medicine

The right treatment for the right person at the right time
Major Drugs Ineffective for Many...

- Hypertension Drugs 10-30%
  - ACE Inhibitors

- Heart Failure Drugs 15-25%
  - Beta Blockers

- Anti Depressants 20-50%

- Cholesterol Drugs 30-70%
  - Statins

- Asthma Drugs 40-70%
  - Beta-2-agonists
...And Harmful to Some

- 100,000 deaths per year
- Just in hospitals: about 6.7% of patients (2.2 million) experience serious adverse drug reactions

Serious adverse drug reactions in even smaller percentages of treated populations have led to the withdrawal of several drugs from the market:

- Zelnorm
- Vioxx
- Cylert
- Rezulin
- Baycol
- Lotronex*

*Reintroduced in 2002 after a very strong campaign from patients who saw it as an important drug that should be made available again, even with restrictions.

“Are good drugs going to the wrong people?”
The Old Paradigm: Treatment of Disease

Reactive Medical Care

Diagnose Disease; Treat Symptoms; Costly, Trial and Error Treatment
Personalized Medicine Paradigm: Health Management

Efficient Medical Care

- Health Management
- Molecular Screening
- Early Detection
- Rapid Effective Treatment
- Improved Quality of Care

Disease Severity

Time

Predisposition
Screening
Diagnosis/Prognosis
“Right” Drug
Monitoring
Personalized Medicine Paradigm: Moving Healthcare Upstream

Preventive Medical Care

Predisposition Guides Prevention; Treat the Molecular Markers vs. Symptoms and Disease; Healthcare Cost Reduction
Personalized Medicine
In Research & Development

Safer, More Effective Drugs
Identify disease targets, speed clinical trials, and advance more drugs that are safe and effective for specific populations

- Faster path to disease targets using genetic data
- Speed trials by testing on patients selected for likely high response and safety

Knowledge of biological pathways and gene variants helps eliminate poor candidates

Target optimal population by combining drug with molecular diagnostic test
What Drives the Movement to Personalized Medicine?

**Consumer Demand for:**

**Safer, More Effective Drugs**
End of one-size-fits-all drugs. New drugs will be safe and effective for specific populations.

**Faster Time to a Cure**
Using genomic information to find disease targets. Speedier clinical trials based on high responder population.

**Cost-Effective Healthcare**
Reduced costs, due to avoidance of futile treatments and improved clinical outcomes.
"The challenge for us as an industry ... is to move more from a blockbuster model to a targeted model. We need a better value proposition than today."

Sidney Taurel
Chairman, President and CEO
Eli Lilly and Company
It’s Already Here...
In the Media

January 3
Test Could Gauge Risk in Patients with Lung Cancer

March 18

The New York Times
February 7
“Test to Predict Breast Cancer Relapse is Approved”

The Boston Globe
May 21
“Genome-wide Association Research Speeds Discoveries”

February 14
“Kaiser Wants 2 Million Enrollees to Enter Genetic Research Program“

The New York Times
June 19
“On the Horizon, Personalized Depression Drugs”
<table>
<thead>
<tr>
<th>Variable Target</th>
<th>Therapy/Prevention</th>
<th>Disease</th>
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<tbody>
<tr>
<td>Alpha-adducin</td>
<td>ACE inhibitors</td>
<td>Hypertension</td>
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<td>CETP</td>
<td>HMG-CoA reductase inhibitors</td>
<td>Atherosclerosis</td>
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<td>CYP2C9/VKORC1</td>
<td>Warfarin</td>
<td>Coagulation disorders</td>
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<td>Transcriptional profiles</td>
<td>Chemotherapy protocols</td>
<td>Non-Hodgkin’s lymphoma</td>
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<td>Chemotherapy protocols</td>
<td>AML Leukemia</td>
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<td>OncoVue® (117 loci)</td>
<td>Surveillance</td>
<td>Sporadic breast cancer</td>
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<tr>
<td>KRAS mutation</td>
<td>Tyrosine kinase inhibitors</td>
<td>Lung cancer drug resistance</td>
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### It’s Already Here ... in Clinical Practice

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<tbody>
<tr>
<td>BCR-abl; c-KIT</td>
<td>Gleevec/Imatinib</td>
<td>Cancer/Chronic myelogenous leukemia</td>
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<td>BRCA1/2</td>
<td>Surveillance; tamoxifen; prophylactic surgery</td>
<td>Breast and ovarian cancer</td>
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<td>EGFR</td>
<td>Tarceva, Iressa</td>
<td>Lung cancer</td>
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<td>Estrogen receptor</td>
<td>Tamoxifen</td>
<td>Breast cancer</td>
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<td>HER-2/neu receptor</td>
<td>Herceptin/Trastuzumab</td>
<td>Breast cancer</td>
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<td>PML-RAR alpha</td>
<td>Tretinoin/All trans retinoic acid</td>
<td>Acute Myelocytic Leukemia</td>
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<td>p16 gene/CDKN2A</td>
<td>Surveillance</td>
<td>Melanoma</td>
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<td>TPMT</td>
<td>Mercaptopurine</td>
<td>Acute Lymphocytic Leukemia</td>
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<td>TruGene®-HIV 1 Genotyping</td>
<td>Anti-retroviral drugs</td>
<td>HIV virus drug resistance</td>
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<td>Oncotype DX: 16 gene profile</td>
<td>Chemotherapy protocols</td>
<td>Breast cancer recurrence</td>
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<tr>
<td>MammaPrint 70-gene profile</td>
<td>Aduvant chemotherapy</td>
<td>Breast cancer recurrence</td>
</tr>
<tr>
<td>Familion® 5-gene profile</td>
<td>Pharma/Lifestyle prevention</td>
<td>Cardiac rhythm abnormalities/side effects</td>
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<tr>
<td>AlloMap® gene profile</td>
<td>Immunosuppressive drugs</td>
<td>Heart transplant rejection</td>
</tr>
<tr>
<td>Amplichip® CYP2D6/2D19</td>
<td>~25% of prescribed drugs</td>
<td>Various diseases – drug metabolism</td>
</tr>
<tr>
<td>UGT1A1</td>
<td>Camptosar® (irinotecan)</td>
<td>Colon cancer</td>
</tr>
<tr>
<td>Sprycel (dasatinib)</td>
<td>BCR-Abl</td>
<td>Gleevec resistance</td>
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Personalized Medicine: How Will It Affect Healthcare?
Changing Role of the Patient

- Greater knowledge of one’s genetic risks
- Actionable lifestyle and nutrition Rx for reducing risk of disease
- Greater control and patient-centered access to medical records
- Treatment decisions will be improved by an educated patient
- Genetic information affects every aspect of the individual’s life
Changing Role of the Healthcare Provider

- Physician as manager, rather than repository of medical knowledge
- Greater reliance on IT for decision support
- Increased use of molecular tests
- Highly networked medical care
- Healthcare management based on pro-active treatment and longer term outcomes
- New ethical and legal issues/quandaries
New Business Strategies for Pharma

- Uncertain economics of drug development and commercialization
- Regulatory mandates could disrupt development budgets and market plans
- “Personalization” of drugs may affect product lifecycle
- Changing paradigm for marketing and sales of pharmaceutical products. Greater focus on patient education emphasizing proactive care, prevention, and targeted treatments.
New Business Strategies for Clinical Laboratories

- Increase emphasis on proactive testing for pre-symptomatic individuals
- Educate physicians and patients to capitalize on new genetic/molecular tests
- Promote standardization of analytical genomic/proteomic technologies, sample collection, handling and storage
- Work with diagnostics developers to establish outcomes evidence for emerging tests
Personalized Medicine Coalition:

An Agent of Change
Convening Stakeholders and Aligning Objectives

The Personalized Medicine Coalition (PMC), representing a broad spectrum of academic, industrial, patient, provider, and payer communities, seeks to advance the understanding and adoption of personalized medicine concepts and products for the benefit of patients.
The potential impact of Personalized Medicine is very broad and far-reaching. There are an array of issues facing us:

- Intellectual property
- Regulatory oversight
- Reimbursement
- Privacy / Ethics
- Healthcare insurance
- Patient education
- Physician education
- Hospital system infrastructure
- R&D incentives
Major Policy Initiatives

- **Genetic privacy** – building confidence among the public to ensure widespread acceptance of genetics in medical care

- **Regulation** – paving the way for market approval of personalized medicine drugs and diagnostics

- **Reimbursement** – ensuring coverage of predictive diagnostics, and targeted treatments for a new paradigm of healthcare

- **R&D Business Incentives** – creating incentives for R&D to generate a stream of linked diagnostics and therapeutics

- **Investment** – increasing government funding for basic and translational research
According to polls conducted on genetic privacy:

- 93% of Americans believe that if someone has had a genetic test, their employer should not be able to use the information in hiring or promotion, and their insurer should not use the information to reduce benefits or increase prices (Genetics and Public Policy Center, Johns Hopkins University, 2007)

- 76% of Americans think Congress should protect genetic information (Genetics and Public Policy Center, Johns Hopkins University, 2007, Research!America, 2006)

Genetics Information Non-discrimination Act (GINA) passes US House by a vote of 420-3 (April 25, 2007)
Genetic Privacy and Protection

Encourage use of genetic services and participation in clinical trials.

- Support passage of the Genetic Information Non-discrimination Act (GINA)
- Define patient and healthcare worker access and control of electronic medical records
- Ensure protections against insurer and employer discrimination are enforceable
- Monitor public attitudes toward genetic testing to measure progress
Regulation

Create a more predictable regulatory environment that keeps pace with scientific advances and evolving business models.

- Ensure new regulations encourage innovation. Support the US FDA Guidance on voluntary PGx data submissions
- Advocate for continued guidance on Rx/Dx co-development
- Advocate for guidance on voluntary post-approval surveillance of drugs, when genetic information on ADRs and efficacy emerge
- Promote global regulatory harmonization on the FDA model of PGx data submissions
Reimbursement - Diagnostics

Place reimbursement on a sound economic footing. Diagnostics comprise 5% of hospital costs, yet leverage 70% of healthcare decisions.

• Increase level of reimbursement for molecular diagnostic tests under the physician fee schedule vs. laboratory fee schedule
• Create incentives for insurance industry to reimburse preventive testing and treatments
• Support new formulary models that incorporate concepts of genetic segmentation on safety and efficacy, and preventive treatment
• Shift from focus on short-term healthcare and unit costs, to long-term costs and outcomes
• Demonstrate and communicate savings in doctor visits, length of hospital stay and other medical procedures
Encourage industry to develop personalized medicine products through incentives in regulation, patenting and other areas of government policy.

Encourage industry to develop personalized medicine products by establishing public policies that:

- Credit companion diagnostics R&D
- Authorize funds for companion diagnostic development
- Streamline the FDA approval process for companion diagnostics
- Accelerate the reimbursement of companion diagnostics
Invest in proteomics, genomics, imaging and other technologies that are essential to meet the need for validated biomarkers.

- Support full funding of NIH
- Support programs in basic research
- Support programs that translate basic research into clinical therapeutics, diagnostics and methods for prevention
## PMC Member Organizations

### Research and Educational Institutions
- AACC (American Association of Clinical Chemistry)
- American Institute for Medical and Biological Engineering (AIMBE)
- American Society of Human Genetics (ASHG)
- Bentley College
- The Brain Institute at the University of Utah
- Center for Molecular Medicine
- Cincinnati Children’s Hospital Medical Center
- Cleveland Clinic Genomic Medicine Institute
- The Critical Path Institute (C-Path)
- Duke University
- Genetics, Ethics & Policy Consulting
- The George Washington University Medical Center
- Harvard-Partners Center for Genetics and Genomics
- Hudson-Alpha Institute for Biotechnology
- Institute for Genomics & Systems Biology, The University of Chicago and Argonne National Laboratory
- Karolinska Institute
- Marshfield Clinic
- Mayo Clinic
- National Coalition for Health Professional Education in Genetics (NCHPEG)
- The Ohio State University Medical Center
- National Jewish Medical and Research Center
- PENN Medicine
- Vanderbilt University Medical Center

### Strategic Partners
- Boston Healthcare Associates, Inc.
- Center for Medicine in the Public Interest
- Clear Point Health
- Defined Health
- Diaceutics
- Feinstein Kean Healthcare
- Genomic Healthcare Strategies
- IDA Ireland
- KFDunn Life Sciences, a division of Aloysius Butler & Clark
- Nixon Peabody LLP
- PAREXEL International
- Personalized Medicine Partners, LLC
- Pri-Med Institute
- Wilson Sonsini Goodrich & Rosati

### Venture Capital
- Boston Millennia Partners
- Burrill & Company
- Kleiner, Perkins, Caufield & Byers
- MDV-Mohr Davidow Ventures
- Pappas Ventures
- Stephens Investment Management

### Health Insurance
- Aetna
- WellPoint

### Industry & Trade Associations
- American Clinical Laboratory Assoc.
- PhRMA

### Emerging Biotech/Pharma
- Perlegen Sciences, Inc
- Xanthus Life Sciences, Inc.

### Consumer Genetic Testing
- DNA Direct, Inc.
# PMC Member Organizations

## Diagnostics
- Aureon Laboratories, Inc.
- Aviir
- BG Medicine
- Bio Research Support, Inc.
- The Brain Resource Company Limited
- dnaPrint Genomics, Inc.
- DNA Vision SA
- Exagen Diagnostics, Inc.
- Expression Analysis, Inc.
- Genomas, Inc.
- Genomic Health, Inc.
- Gentris Corporation
- Lipomics Technologies, Inc.
- Monogram Biosciences
- Nanosphere, Inc.
- NeuroMark
- Pathway Diagnostics
- PGx Health (a division of Clinical Data, Inc.)
- TheraGenetics Ltd.
- XDx, Inc.

## IT/Informatics
- IBM Healthcare and Life Sciences
- Lead Horse Technologies
- Mirixa
- Saffron Technology, Inc.
- Theranos, Inc.

## Clinical Laboratories
- Kimball Genetics, Inc.
- LabCorp
- Quest Diagnostics

## Patient Advocacy Groups
- Alliance for Aging Research
- FasterCures
- Sarcoma Foundation of America

## Agency Partners
- Centers for Disease Control and Prevention
- Centers for Medicare and Medicaid Services
- National Cancer Institute
- National Human Genome Research Institute
- U.S. Food and Drug Administration

## Research Tools
- Affymetrix, Inc.
- Applera Corporation
- Applied Biosystems
- Celera
- Gene Logic
- GenVault Corp.
- HistoRx
- Illumina, Inc.
- Luminex Corporation
- Nanogen, Inc.
- Osmetech Molecular Diagnostics
- Qiagen, Inc.

## Large Biotech/Pharma
- Abbott Molecular Inc.
- AstraZeneca Pharmaceuticals
- Eli Lilly and Company
- Genzyme Corporation
- Johnson & Johnson Pharmaceutical Research & Development LLC
- Millennium Pharmaceuticals, Inc.
- Pfizer, Inc.

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[www.PersonalizedMedicineCoalition.org](http://www.PersonalizedMedicineCoalition.org)
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The Personalized Medicine Coalition

To learn more, visit:

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### Personalized Medicine Review

**Choose the best answer**

- **What are benefits of Personalized Medicine?**
  1. Treatment tailored to individual’s genetics
  2. One physician for each patient
  3. Each individual has sequenced DNA

- **What is the estimated number of deaths due to adverse drug reactions?**
  1. 5 million per year
  2. 100,000 per year
  3. 1,000 per year

- **Why would genetic characterization prior to therapy reduce the time to disease response to treatment?**
  1. Drugs would be more effective
  2. Drugs would be used only for the genotype for which they were designed
  3. Optimum dosage could be assigned.

- **Why would genetic characterization reduce the incidence of adverse events?**
  1. Drugs would be less toxic
  2. Drugs would be used only for the genotype for which they were designed
  3. Pharmaceutical companies would be required to market safer drugs.
• What are benefits of Personalized Medicine?
  1. Treatment tailored to individual’s genetics

• What is the estimated number of deaths due to adverse drug reactions?
  1. 100,000 per year

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