Personalized Medicine: Dead or Alive?

BioNJ Diagnostic & Personalized Medicine Innovation Summit and Funding Roundtable

March 14, 2012
Princeton University
Princeton Township, New Jersey

G. Steven Burrill
Chief Executive Officer
Burrill & Company
Burrill & Company’s 26th annual report on the life sciences industry

Available Later this Month
And a CD of the first 25 years of publications

Available at www.burrillandco.com
Markets off to a Strong Start in 2012

- Unemployment dropped to 8.3 percent in January, its lowest level since February 2009
- Dow Jones Industrial Average closes above 13,000 for the first time since 2008
- The Nasdaq Composite Index hits a high not seen since December 2000
- Burrill Select Index up more than 15 percent for the year
### Political and Economic Turmoil Turned Markets in H2 2011

<table>
<thead>
<tr>
<th>INDEX</th>
<th>H1 2011 % Change</th>
<th>H2 2011 % Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burrill Select</td>
<td>11.00%</td>
<td>-10.45%</td>
</tr>
<tr>
<td>Burrill Large Cap</td>
<td>17.30%</td>
<td>5.57%</td>
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<tr>
<td>Burrill Mid-Cap</td>
<td>29.80%</td>
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<tr>
<td>Burrill Small-Cap</td>
<td>9.50%</td>
<td>-14.23%</td>
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<tr>
<td>Burrill Diagnostics</td>
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<tr>
<td>Burrill Personalized Medicine</td>
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<td>-9.40%</td>
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<tr>
<td>Burrill Biogreentech</td>
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<tr>
<td>Nasdaq Composite</td>
<td>4.50%</td>
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<tr>
<td>Dow Jones Industrial Average</td>
<td>7.20%</td>
<td>-2.90%</td>
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<tr>
<td>Amex Biotech</td>
<td>12.60%</td>
<td>-26.10%</td>
</tr>
<tr>
<td>Amex Pharmaceutical</td>
<td>8.60%</td>
<td>-0.50%</td>
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</tbody>
</table>
## Indices Post Solid Gains in First Two Months of 2012

<table>
<thead>
<tr>
<th>INDEX</th>
<th>Performance in 2011</th>
<th>First Two Months 2012</th>
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<tbody>
<tr>
<td>Burrill Select</td>
<td>18.5%</td>
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<tr>
<td>Burrill Large Cap</td>
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<tr>
<td>Burrill Diagnostics</td>
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<tr>
<td>Burrill Personalized Medicine</td>
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<tr>
<td>Burrill Biogreentech</td>
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<tr>
<td>Nasdaq Composite</td>
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<td>14.7%</td>
</tr>
<tr>
<td>Dow Jones Industrial Average</td>
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<td>5.8%</td>
</tr>
<tr>
<td>Amex Biotech</td>
<td>-16.0%</td>
<td>20.4%</td>
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<tr>
<td>Amex Pharmaceutical</td>
<td>8.9%</td>
<td>0.5%</td>
</tr>
</tbody>
</table>
Tough Year for IPOs, But Investors Win Big Through M&A

• IPOs got done, but activity slowed in the second half of 2011 (16 in 2011 vs. 20 in 2010)

• Companies sold more share and raised less money than they hoped

• Aftermarket performance weak

• Big winners in M&A companies with early- and mid-stage assets demanded big premiums
The Challenge of Personalized Medicine

• Is personalized medicine a surrogate for molecular diagnostics?

• Will our understanding of genomics / proteomics / metabolomics really improve treatment by getting the right drug to the right patient at the right dose and the right time?

• Can we be predictive? Are we preemptive?

• Is value actually created?

• Are providers using it? Are patients demanding it?

• Are payers willing to pay for it?
What are the pressures on healthcare and does personalized medicine provide an answer?
“The Greatest Demographic Upheaval in Human History.”

- Dramatic reductions in mortality
- Marked reductions in fertility

Source: David Bloom, 7 Billion and Counting, Science
World Population Hits a Milestone

The number of people on the planet breaks the 7 billion mark

United Nation's population projections by location

- World
- Asia
- Africa
- Europe
- Latin America
- Northern America
- Oceania

Projected
More Than 9 Billion People by 2050

World population will grow from 6,927,372,294 to 9,149,984,000

32.4% Increase

Source: Scientific American
First Baby Boomer turned 65

• Baby boomers born between 1946 and 1965

• About 10,000 baby boomers will turn 65 every day

• Last baby boomer will turn 65 in 2030
Increasing longevity and slowing birth rates is raising the age of population across the globe

Source: World population prospects, 2008 Revision, United Nations
Patients seeing ten or more doctors during the last six months of life

End of Life Care Costly in the United States

Source: Dartmouth Atlas Project
Big Spenders: Elderly in U.S. Make Up 43% of Top Decile

Distribution of population by persistence of health care expenditures and age, in the U.S. civilian noninstitutionalized population, 2008 to 2009.

These Trends Fuel the Rise of Chronic Disease

Costliest Chronic Diseases Associated with Aging

75% of Total Cost

Cardio-vascular Diseases: 33%
Cancer: 20%
Diabetes: 11%
Over-weight & Obesity: 10%
Other Chronic: 9%
All Other: 17%
Total Healthcare Cost: 100%

75% of Total Cost:

Cardio-vascular Diseases: $653 billion
Cancer: $396 billion
Diabetes: $226 billion
Over-weight & Obesity: $209 billion
Other Chronic: $190 billion
All Other: $342 billion
Total Healthcare Cost: $2,106 billion

Source: CDC, US Department of Health & Human Services
Rise in Chronic Disease Fueling Healthcare Costs

*Projections
As Costs Rise, Governments Demand Value for Their Money

Pricing pressures will alter pharmaceutical development strategies

• Germany’s new drug pricing law AMNOG
• US’s Independent Payment Advisory Board
• UK’s National Institute for Health and Clinical Excellence
What’s Ailing the Healthcare Systems?

• Rise of chronic disease
• Aging population
• Rising demand vs. finite resources
• Unhealthy behavior difficult to change
• Focus on treating, rather than preventing disease
• Innovation too often drives rather than lowers costs
• Unhealthy behavior difficult to change
• One-size-fits-all medicine not the most effective way to treat people
The World Today: Safe and Effective

One Size Does Not Fit All

PATIENTS CAN RESPOND DIFFERENTLY TO THE SAME MEDICATION

- **ANTI-DEPRESSANTS (SSRIs)**: 38%
- **ASTHMA DRUGS**: 40%
- **DIABETES DRUGS**: 43%
- **ARTHRITIS DRUGS**: 70%
- **ALZHEIMER’S DRUGS**: 70%
- **CANCER DRUGS**: 75%

*percentage of the patients for which a particular drug in a class is ineffective, on average*
Billions Wasted On Ineffective Therapies

At a time when payers are looking to stop spending on drugs that don’t work, personalized medicine provides a way to filter out ineffective therapies for certain patients

• An estimated 90 percent of drugs only are effective in 30 percent to 50 percent of the population

• Global drug sales reached $825 billion in 2010

• Estimated $352.1 billion spent on ineffective drugs globally in 2010
How Personalized Medicine Can Address these Problems

• Shift medicine from focus on treating illness to prevention

• Help provide early intervention to treat problems when they are least costly

• Avoid waste on ineffective medicines
Policy and operation challenges interfere with the benefits of personalized medicine being realized. These include:

- Health information technology is not interoperable
- Inconsistent coding and language standards
- Problems in data sharing
- Weak feedback loops
- Privacy concerns
- Ineffective reimbursement problems

Source: Darrell M. West Enabling Personalized Medicine through Health Information Technology: Advancing the Integration of Information, The Brookings Institution
What Drives Personalized Medicine?

Patients: Demanding safe, more effective drugs.

Doctors: Don’t want trial and error approach to Medicine.

Drugmakers: Want to cut cost and time out of drug development and remove regulatory uncertainty.

Regulators: Increasingly demanding that drugmakers identify patients for which a given drug works.

Payers: Don’t want to pay for treatments that don’t work or justify expense.
Personalized Medicine Under Attack

• Are we chasing an elusive dream?

• Has enthusiasm for building businesses outpaced our scientific understanding?

• What is the business model that works?
“For biologist, the genome has yielded one insightful surprise after another. But the primary goal of the $3 billion Human Genome Project—to ferret out the genetic roots of common diseases like cancer and Alzheimer’s and then generate treatments—remains largely elusive. Indeed after 10 years of effort, geneticists are almost back to square one in knowing where to look for the roots of common disease.”

Nicholas Wade
The New York Times
July 7, 2011
Et tu, Craig J?

Why is it taking so long for the results of genome research to be applied in medicine?

Because we have, in truth, learned nothing from the genome other than probabilities. How does a 1 or 3 percent increased risk for something translate into the clinic? It is useless information.

J. Craig Venter in an interview with Der Spiegel
July 29, 2010
The Criticism

A number of cases in recent years have raised questions about molecular diagnostics

“Why don’t we have assays out there, with this enormous promise? It’s either because these things just don’t work, or because we’ve used sloppy science to test them.”

Dan Hayes
Breast cancer researcher at the University of Michigan
The Duke Case

- Clinical trials to test personalizing cancer therapies based on flawed research
- Charges of mismanagement, shoddy science and fraud
- Scientific papers retracted, discredited researcher resigns
- Investigations by Duke, the National Cancer Institute, and the Institute of Medicine underway
- Lawsuit filed by patients and families
“While researchers agree there is great promise in this science, it has yet to yield many reliable methods for diagnosing cancer or identifying the best treatment. Instead, as patients and their doctors try to make critical decisions about serious illnesses, they may be getting worthless information that is based on bad science.”
Rising retraction rates suggest that more published findings are unreliable cannot be replicated or are simply wrong.

**Retractions increasing...**

<table>
<thead>
<tr>
<th>FIELD</th>
<th>RETRACTIONS</th>
<th>2001-05</th>
<th>2006-10</th>
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<tbody>
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<td>Medicine</td>
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<td>Biology</td>
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<td>Chemistry</td>
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<td>Neuroscience</td>
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<td>Immunology</td>
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<td>Physics</td>
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<tr>
<td>Materials</td>
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</tbody>
</table>

**...including at most influential journals...**

<table>
<thead>
<tr>
<th>JOURNAL (ranked by citations)</th>
<th>RETRACTIONS</th>
<th>2001-05</th>
<th>2006-10</th>
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</thead>
<tbody>
<tr>
<td>Journal of Biological Chemistry</td>
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<tr>
<td>Proceedings of the National Academy of Sciences of the USA</td>
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<tr>
<td>Nature</td>
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<tr>
<td>Science</td>
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<tr>
<td>Journal of the American Chemical Society</td>
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<tr>
<td>Physical Review Letters</td>
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<tr>
<td>New England Journal of Medicine</td>
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<td></td>
<td>5</td>
</tr>
<tr>
<td>Physical Review B-Conondensed Matter</td>
<td>7</td>
<td></td>
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<tr>
<td>Astrophysical Journal</td>
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<tr>
<td>Applied Physics Letters</td>
<td>4</td>
<td>5</td>
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</tbody>
</table>

Sources: Thomsom Reuters (retractions by field and journal); R. Grant Steen, Journal of Medical Ethics, Dec 2010 (retraction time)
08/10/11: WSJ reports the # of papers published in research journals have increased 44% since 2001, while # of retractions have grown 15 times.

- Data was compiled by Thomson Reuters Web of Sciences, from index of 11,600 peer reviewed journals.

- The newspaper found 339 retractions in 2010, compared 22 in 2001.

*Based on an analysis of 742 medicine and biology papers retracted from the PubMed database.

Sources: Thomson Reuters (retractions by field and journal); R. Grant Steen, Journal of Medical Ethics, Dec 2010 (retraction time)
Despite the problems, personalized medicine is already transforming medical practice.
We Are Moving to an Age of Genomic Medicine

<table>
<thead>
<tr>
<th>PAST</th>
<th>FUTURE</th>
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<tbody>
<tr>
<td>DISEASE DEFINITION BY SYMPTOMS</td>
<td>MECHANISM</td>
</tr>
<tr>
<td>UNIFORMITY OF DISEASE</td>
<td>HETEROGENEITY</td>
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<tr>
<td>UNIFORMITY OF PATIENTS</td>
<td>VARIABILITY</td>
</tr>
<tr>
<td>UNIVERSAL TREATMENT</td>
<td>INDIVIDUALIZED THERAPY</td>
</tr>
<tr>
<td>SICKNESS</td>
<td>PREDICTIVE/PREVENTATIVE CARE</td>
</tr>
</tbody>
</table>

Source: Burrill & Company
A Transformation of Medicine

Personalized medicine has changed the way doctors think about disease. Rather than viewing disease in terms of its symptoms, it approaches disease from its underlying molecular mechanism driving the disease.
Cancer Redefined

Percentage of patients whose tumors were driven by certain genetic mutations that could be targets for specific drugs, by type of cancer

- Melanoma: 73%
- Thyroid: 56%
- Colorectal: 51%
- Endometrial: 43%
- Lung: 41%
- Pancreatic: 41%
- Breast: 32%
- Other gynecological: 31%
- Genitourinary: 29%
- Other gastrointestinal: 25%
- Ovarian: 21%
- Head and neck: 21%

Source: M.D. Anderson Cancer Center, WSJ
Personalized Medicine Is Improving Diagnosis and Treatment

Blood cancers are revolutionized by an understanding of the molecular mechanisms driving the different forms of the disease.

100 YEARS AGO
- Disease of the blood

80 YEARS AGO
- Leukemia of lymphoma

60 YEARS AGO
- Chronic leukemia
- Acute leukemia
- Preleukemia
- Indolent lymphoma
- Aggressive lymphoma

TODAY
- 38 Leukemia Types Identified
- 51 Lymphoma Types Identified

Source: Genzyme Genetics
Doctors Want to Know More, But Have Little Training

Percent of doctors who have received any genomic-based medicine training:

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Medical School:</td>
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<tr>
<td>percent</td>
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<tr>
<td>Post-Medical School:</td>
<td>42</td>
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<tr>
<td>percent</td>
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<tr>
<td>Neither:</td>
<td>50</td>
</tr>
<tr>
<td>percent</td>
<td></td>
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</table>

Source: CAHG survey of 801 physicians conducted in July-August 2010
Rapidly Falling Cost of Sequencing Opens New Possibilities

Baseline information
Cost of genome sequencing compared with Moore’s Law for computers

Source: Broad Institute
The $1,000 Genome Arrives Now

• Life Technologies Ion Torrent releases machine it says will be able to sequence whole human genomes for $1,000 by end of year

• Price point will allow large sequencing projects that can uncover new understanding of disease and improve drug development

• Scientists say the problem, though, is not cost. Rather its how to deal with all the data
Pharma Improves Drug Development

Personalized medicine helps produce safer, more effective drugs

- 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 help eliminate poor candidates
- Target optimal population by combining drug with molecular diagnostic testing

Source: Personalized Medicine Coalition
Making New Treatments Possible: Genentech’s Herceptin

Late-stage clinical trial:

Without screening for patients who were HER2-positive, Genentech would have had to enroll 2,000 patients over 10 years to show a statistically significant benefit.

By narrowing the focus to a smaller population more likely to benefit, the trial included just 400 patients over 18 months.
Amgen’s Vectibix for Colon Cancer

European regulators rejected the colon cancer drug in 2007 because of weak results.

Amgen submits additional data that uses biomarker to eliminate patients resistant to the drug.

By eliminating resistant patients, the company was able to demonstrate a high enough response rate to satisfy regulators.
“New biomarkers which can identify the patient sub-populations most likely to have a positive response or an adverse reaction to a drug can be applied to applications that never made it through the FDA review process. By viewing the data from unsuccessful past trials through the lens of new biomarkers, it may be possible to turn past failures into future successes.”

Margaret Hamburg
FDA Commissioner
AAAS – The Future of Personalized Medicine
October 26, 2009
Genentech’s Avastin

• Won accelerated approval in 2008 for use in breast cancer patients

• In 2011, the FDA revoked Roche's right to market Avastin as a treatment for metastatic breast cancer saying studies no longer supported its use

• The decision could put a $1 billion dent in Avastin's global sales

• FDA said it is interested in learning whether there may be a subset of patients with breast cancer in which Avastin may provide clinical benefit

• Roche conducting studies to identify such patients
Changes are under way
## Changing Roles of Doctors

<table>
<thead>
<tr>
<th>Past</th>
<th>Future</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unquestioned authorities</td>
<td>• Health advisers</td>
</tr>
<tr>
<td>• Trial and error</td>
<td>• Data driven decisions using health IT and diagnostics</td>
</tr>
<tr>
<td>• Treat disease</td>
<td>• Focus prevention and wellness</td>
</tr>
<tr>
<td>• Disconnected from others in the healthcare system</td>
<td>• Integrated with specialists, labs, and pharmacists</td>
</tr>
</tbody>
</table>
## Changing Roles of Patients

<table>
<thead>
<tr>
<th>Past</th>
<th>Future</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Passive about healthcare</td>
<td>• Active managers of their healthcare</td>
</tr>
<tr>
<td>• Armed with family history</td>
<td>• Armed with knowledge of genetic risks</td>
</tr>
<tr>
<td>• Relied on doctors to maintain health records</td>
<td>• Have access to their own digital health records</td>
</tr>
<tr>
<td>• Relied on doctors as primary source of medical information</td>
<td>• Rely on Internet, social networks, for medical information</td>
</tr>
<tr>
<td>• Received annual check-up</td>
<td>• Monitors health and wellness with digital devices</td>
</tr>
</tbody>
</table>
Payers and Patients Will Play Bigger Role

Traditionally doctors had most of the power in healthcare decision making. Pharmaceutical companies now must operate in a world where payers and patients have greater influence.

Source: Management Center Europe
# Healthcare Systems Are Changing Globally

<table>
<thead>
<tr>
<th>Past</th>
<th>Future</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acute care</td>
<td>• Chronic care (to wellness care)</td>
</tr>
<tr>
<td>• People/dying patients</td>
<td>• Systems/Software</td>
</tr>
<tr>
<td>• Place (hospitals)</td>
<td>• Consumer digital health</td>
</tr>
<tr>
<td>• Payment: Cost-based care</td>
<td>• Value based care</td>
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</tbody>
</table>

- Payment: Cost-based care
- Acute care
- People/dying patients
- Place (hospitals)
- Chronic care (to wellness care)
- Systems/Software
- Consumer digital health
- Value based care
Personalized Medicine: Biotech’s Big Opportunity

We are in early days for targeted therapies

• Existing medicines address only some 150 different targets

• There are more than 2 million proteins in the human body, of which many potentially can cause diseases

• Roche’s Severin Schwan says, “We are only scratching the surface.”
The Challenge

- We are getting good at understanding our genetic risks for diseases, but how can we use that information to prevent disease?

- Healthcare remains disconnected, relies on brick-and-mortar infrastructure and paper records

- Chronic disease management suffers from low compliance

- Mobile technologies can be leveraged to close the infrastructure and personnel gap in developing countries can closed by leveraging mobile technologies

- Healthcare spending is spiraling out of control worldwide
“Nothing has changed clinical practice more fundamentally than one recent innovation: the Internet. Its profound effects derive from the fact that while previous technologies have been fully under doctors’ control, the Internet is equally in the hands of patients. Such access is redefining the roles of physician and patient.”

Pamela Hartzband & Jerome Groopman
New England Journal of Medicine perspective piece in March 2010
Social Networking Takes Hold

5.3 BILLION MOBILE DEVICES

In millions:
- Facebook: 845
- Skype: 663
- Weibo: 480
- Twitter: 462
- Gmail: 364
- Hotmail: 273
- Friendster: 193
- Yelp: 110
- Foursquare: 110
- OpenTable: 22
- Myspace: 10
- LinkedIn: 50
- Orkut: 11
- Badoo: 11
- Qzone: 10

Source: JESS3 via TechCrunch, May 2011
Heal Thyself

Percent of people who say they have used social media for healthcare purposes

Source: PwC Health Research Institute
But what’s the quality of the information you get?

On the Internet, Nobody Knows You’re a Dog
Technology is evolving rapidly through innovation
Innovation Takes Many Forms

• New ideas, new products
  – Fax
  – GPS
  – Email
  – WebMD

• Changing existing products with new features/new industries
  – US mail → FedEx
  – Diagnostic test → “Onco-type Dx” (personalized medicine)
  – Rx (“one size fits all”) → Targeted therapeutics (biomarker/mutation based)
Incremental vs. Disruptive Innovation

Incremental innovation
• Better products
• Higher prices
• Driven by competition

Disruptive innovation
• Technological simplicity
• Initially worse functionality
• Fundamentally simpler
• Driven by need
Healthcare Pricing Pressure Force Disruptive Innovation

Japan mandates lower prices for services when volumes increase

• Demand for MRI scans forced prices to drop to less than $100 for each scan

• Rather than cease innovating, manufacturers developed low-powered MRI machines

• Toshiba created a unit that uses less magnetic strength, lower-resolution, less computing power, but sells for less than $200,000

• That compares to multi-million price tag in the United States for MRI machines
Rapidly Developing Technologies Will Impact Healthcare

- High-speed, low-cost genomic sequencing
- Artificial intelligence
- Robotics
- Smart pills
- Stem cells
- Gene therapy
- Systems biology/synthetic biology
- Cheap/global access to internet (connectivity)
- Mobile phone Apps
- 24/7 body wearable monitors
- Telemedicine/telehealth

Source: Medwonder.com
## Evolution of Everyday Technology is Rapid

<table>
<thead>
<tr>
<th>From the Old</th>
<th>To the New</th>
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<tbody>
<tr>
<td>Broadcast Television</td>
<td>On Demand Viewing</td>
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<tr>
<td>Bank Teller, credit cards</td>
<td>ATMs, pay by cell phone</td>
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<tr>
<td>Personal Computer</td>
<td>Tablet</td>
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<tr>
<td>Hard Drives</td>
<td>The Cloud</td>
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<td>Apps</td>
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<td>Clinical Testing and Monitoring</td>
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<td>Fossil Fuel</td>
<td>Renewable Fuel</td>
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<tr>
<td>Incremental Innovation</td>
<td>Disruptive Innovation</td>
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We Are Living in Exponential Times

<table>
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<th>Technology</th>
<th>Years to reach 50 million consumers</th>
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<tr>
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</table>

*Years to reach 50 million consumers*
Big Trends: The Promise of Mobile Technologies for Health

Source: World Bank, world Development Indicators, U.N. telecommunications agency, Kaiser Family Foundation
The Smartphone at the Center of a Digital Health Revolution

• More than 80 percent of U.S. physicians own a smartphone or tablet device

• Physicians embrace mobile monitoring for their patients

• Cell phone-based disease management improves outcomes

• Mobile health solutions present major business opportunities
Physicians Embrace Mobile Monitoring

Percentage of U.S. physicians wanting to monitor patients at home and top priority parameters for remote tracking

No
12%

Yes
88%

65% - Weight
61% - Blood sugar
57% - Vital signs (e.g. blood pressure, heart rate, respiratory rate)
54% - Exercise/physical activity
36% - Calories/fat content taken in
36% - Pain level
35% - Sleep patterns
28% - Cardiac rhythm
17% - Bladder control
16% - Acid reflux/indigestion
13% - Digestive health

Source: PricewaterhouseCoopers HRI Physician Survey, 2010
Healthcare Products are Merging into Consumer Retail

Example:

Alivecor’s iPhone ECG
How Digital Health Changes the World

• Extends reach of healthcare institutions to home

• Cellphone-based disease management improves outcomes

• Patients accept ownership and financial responsibility for better health and wellness tools

• Mobile health solutions present major business opportunities
Digital health can address problems in healthcare through personalization, prediction, and prevention.
What Is Digital Health Doing for Us

• Improving access and delivery of healthcare
• Reducing costs
• Increase compliance
• Personalizing treatment
• Providing better monitoring and information
• Allowing early interventions
• Elderly people able to live independently longer
• Modify behavior
Access and Delivery: California Telehealth Network

• California Telehealth Network will connect more than 800 California healthcare providers in underserved areas

• Addresses challenge for how to provide high-quality access to clinical services, particularly those that are delivered by scarce experts

• People who are in remote areas can avoid having to travel for hours to get access to specialists
Bringing Affordable Technology to Remote Patients: Mobisante

• Mobisante’s ultrasound device works with smartphones and tablets to provide mobile clinical grade ultrasound imaging

• Rural OB/GYN can confirm pregnancy and detect common complications without sending patients to remote centers

• Using the onboard connectivity, diagnostic data can be sent to the hospital prior to patient arrival for better preparation

• Broad applicability in the developing world
Disruptive Innovation: Lark Sleep Monitor

Polysomnography suite

- Expensive
- Requires expert to use
- Limited to institutions
- Not useful for monitoring or screening
- No ongoing feedback

LARK Sleep Monitor and Coach

- Inexpensive ($99 range)
- Consumer and expert use
- Available where needed
- Ideal for monitoring and screening
- Ideal for ongoing feedback
Improving Compliance: GlowCaps

• Reminds patients to take their medication

• Tells doctors when they don’t

• Orders refills before patient runs out

GLOWCAP FEEDBACK LOOP:

Source: Vitality
Personalizing Treatment: Proteus Biomedical

• Computer chip made from food ingredients designed to be co-manufactured with drugs at ultra-low cost

• Delivers medicine combined with information that captures when drugs are taken along with real-time physiological data

• Skin patch collects data from tiny sensors and transmits to cell phone

• Provides better information to doctor and allows patients to better manage chronic conditions
WellDoc turns cell phone into diabetes management tool to improve outcomes.

• Ongoing patient feedback & triggers

• 24/7 insight and course correction

• Connectivity provides information to patient and healthcare provider

• Studies show use of WellDoc improves outcomes
Early Interventions: AT&T Smart Slippers

Lower costs and improve care

Pressure sensors embedded in their soles to transmit foot movement data over AT&T’s network.

Detects if something is wrong with an elderly patient’s gait and alerts a doctor via e-mail or text message

Could prevent a fall and a costly trip to the emergency room
Allow Elderly to Live Independently Longer: Care Innovations

• A range of wellness surveys, brain fitness games and medication compliance reminders

• Access to community news, calendars, and alerts helping live-in and off-campus members to stay engaged

• A simple, secure interface to interact online through a private social network and engage in their physical, social and mental health

• Helps staff monitor the seniors’ wellness and identify potential problems early

• Monitors and assess community participation and individual wellness
Modify Behavior: Keas

• Employer wellness program that promotes health through the use of games

• Uses quizzes, newsfeeds, goal setting and celebration – bonus points for those who live healthily

• Combined with the sense of delight that players can watch each other succeed in diet/exercise programs, and keeps them engaged via social support.

• Keas participants: Lost weight, improved eating habits
Smartphones Push World from Web to Apps

• A total of 220 million Apple iOS and 100 million Android devices sold to date worldwide

• Some 65 percent of the 150 million smartphones projected in the U.S. by end of 2011 will be iOS or Android devices

• Apple’s iTunes Store boasts 14 billion app downloads and Android Market adds another 4.5 billion

• Some 37 percent of all U.S. mobile subscribers use downloaded apps and half access social media and blog sites

• One smartphone generates 24 times the data traffic of one feature phone
So, what does the past year tell us about personalized medicine?
Big Events in Personalized Medicine

• FDA issued new guidance on biomarkers and draft guidance on companion diagnostics

• Next-generation sequencing brings us to the $1,000 genome in 2012

• NIH launches its Genetic Test Registry

• Deal environment heating up – more big dollar acquisitions

• Market for personalized medicine projected to reach $452 billion by 2015 from $232 billion in 2011, according to PwC
New Personalized Medicines Win Approval

- Roche’s melanoma drug Zelboraf approved with companion diagnostic

- Pfizer’s non-small cell lung cancer drug Xalkori with companion diagnostic

- Seattle Genetics’ lymphoma drug Adcetris, a drug that marries an antibody to a toxic chemotherapeutic payload to deliver a targeted therapy to a certain subgroup of lymphoma patients
Roche Makes a $5.7 Billion Hostile Bid for Illumina

Swiss biopharma giant seeks to transform itself into a personalized medicine powerhouse

Company ultimately sees next-generation sequencing a routine test at hospitals and doctors’ offices
The Bad News

• Growing frustration that personalized medicine has overpromised and under-delivered

• Regulatory environment remains challenging

• Difficult to raise money

• Complexity of understanding meaning of genetic information bigger challenge than first thought

• Sloppy science and scandal mars the field
Deal Values Climb, but Number of Transactions Fall

Personalized Medicine Financings 2009-2011

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**Summary:**
Deal values climb, but the number of transactions falls

**Bar Graph Description:**
- **Y-Axis:** Total Deal Value (M)
- **X-Axis:** Year (2009, 2010, 2011)
- **Legend:**
  - Total Deal Value (M)
  - Number of Financings

**Data Points:**
- **2009:**
  - Total Deal Value: $3300 M
  - Number of Financings: 120
- **2010:**
  - Total Deal Value: $3100 M
  - Number of Financings: 80
- **2011:**
  - Total Deal Value: $3400 M
  - Number of Financings: 160

---
Tools and Technology Deals Attract the Biggest Dollars

Personalized Medicine Deal Value of Financings by Focus 2009-2011
Personalized Medicine M&A Values Soar, but Activity Falls
Companion Diagnostics Demand Helps Drive Deals

Personalized Medicine Partnering 2009-2011

<table>
<thead>
<tr>
<th>YEAR</th>
<th>NUMBER OF PARTNERINGS</th>
</tr>
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<tbody>
<tr>
<td>2009</td>
<td>~70</td>
</tr>
<tr>
<td>2010</td>
<td>~80</td>
</tr>
<tr>
<td>2011</td>
<td>~90</td>
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## Companion Diagnostics Deals

### Big Pharma Believes: Announced partnerships during past year

<table>
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<tr>
<th>Licenser</th>
<th>Licensee</th>
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<tbody>
<tr>
<td>Clovis Oncology</td>
<td>Roche</td>
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<tr>
<td>Qiagen</td>
<td>Pfizer</td>
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<tr>
<td>Life Technologies</td>
<td>GlaxoSmithKline</td>
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<td>Medco, United BioSource</td>
<td>Sanofi</td>
</tr>
<tr>
<td>Evotec</td>
<td>Roche</td>
</tr>
</tbody>
</table>
Conclusions and what’s ahead
What’s Ahead

Governments will seek to contain healthcare costs

• Price controls

• Paying for value

• Penalizing unhealthy behavior

Payers are becoming more powerful determinants of development strategies

• Companies need their input early

• Payers will demand not only safety and efficacy, but VALUE!
What’s Ahead

Capital Markets Will Remain Jittery

• Companies will need to be opportunistic in raising capital

• Innovation is still possible to fund and develop

The FDA will move from being a gold-standard to a late adopter

• Regulatory barriers will push innovative companies to seek approvals outside the United States first

• Demands from regulators will push drugmakers to pursue personalized medicine
What’s ahead

Healthcare reform is underway. It is being driven by:

- Patients/Consumers
- Doctors
- Payers
- Technology

Smartphones will become the key connector between people and their healthcare providers

- Increasingly monitor and guide users on their health and wellbeing
- Personalizes treatment, and predicts and prevents disease
- Pulling consumers to adoption.
Digital Health Will Touch All Aspects of Healthcare

Digital health will change the way:

• We access and deliver care

• Enable more personalized healthcare

• Improve decision making by providing better data

• Enhance value by helping distinguish between what works and what doesn’t

• Address drivers of costs in our healthcare system by helping change unhealthy behaviors, improve chronic disease management, and allow for earlier medical interventions before health problems grow costly
We Are at the Beginning

The convergence of technology is bringing about a radical change to all aspects of healthcare.

These changes are placing the patient at the center of healthcare and putting consumers in greater control of their own health than ever before.
The Good News

It will be a difficult environment in 2012, but one with big opportunities for companies that can provide true innovation that addresses issues of:

• Cost

• Access

• Improved efficacy

• Unmet medical needs
What’s the Verdict on Personalized Medicine?

Dead?  
Alive?
Challenges Are Big

- Regulatory pathway still uncertain
- Reimbursement difficult and slow
- Investors reticent from lack of rewards
- Science more complex than originally believed
- Differences between countries increases regulatory and reimbursement challenges
- Perverse incentives slow adoption
- Value capture is the key
But There Are Reasons to Be Encouraged

• Big Pharma is now on board

• FDA believes

• Rapid decline in cost of sequencing will lead to new understanding the relationship between our genes and disease

• The pressure to contain the cost of healthcare will lead to a greater emphasis on personalization, prediction, and prevention

• As payers demand value, personalized medicine will provide the evidence they require

• Value is real — just challenging to get!
More change in the next 10 years than from 1-2010

It will be very different going forward

It’s a globally connected/virtual world of informed and discriminating consumers and government providers/payers all based on value!
Personalized Medicine: Dead or Alive?

BioNJ Diagnostic & Personalized Medicine Innovation Summit and Funding Roundtable

March 14, 2012
Princeton University
Princeton Township, New Jersey

G. Steven Burrill
Chief Executive Officer
Burrill & Company