

# Precision Medicine



**A BUSINESS & MARKETING PERSPECTIVE:  
EXCERPTS AND COMMENTS FROM THOUGHT LEADERS**

**BARBARA SIMKIN  
PHARMADECISIONS LLC**

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# The Power of Precision

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"This is the future of medicine" ..... "There is no turning back. The technology is available and there are already so many targeted therapies.\*"

[\*Dr. Massimo Cristofanilli, Associate Director for Translational Research and Precision Medicine at Northwestern University]

**FIGURE 1: ONE SIZE DOES NOT FIT ALL**

Percentage of the patient population for which a particular drug in a class is ineffective, on average.



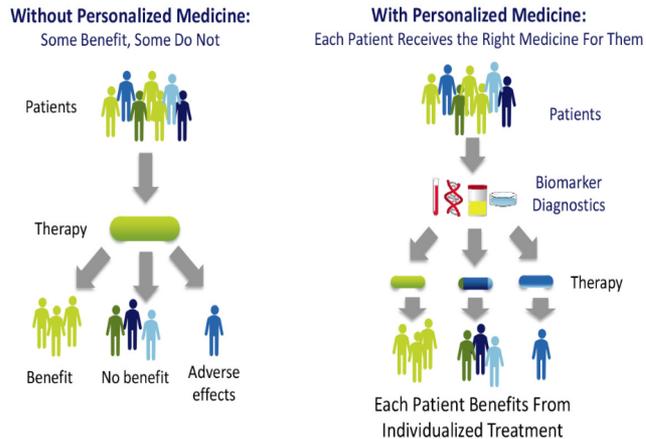
Reproduced with permission from: Spear, BB, Heath-Chiozzi, M, Huff, J. Clinical application of pharmacogenetics. *Trends in Molecular Medicine*. 2001;7(5): 201-204.

# “A New Treatment Paradigm” [PhRMA]

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## A NEW TREATMENT PARADIGM

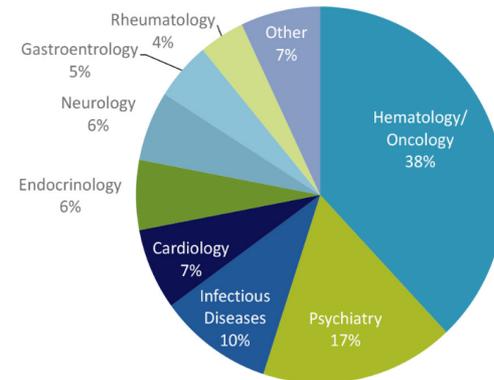
The molecular profile of an individual patient and their disease influences the effect of a medicine. Biomarker diagnostics help to target the right medicine to the right patient.



Source: Adapted from Bayer Healthcare, "Personalized Medicine." (accessed May 2015).

## PERSONALIZED MEDICINES ARE BENEFITTING PATIENTS ACROSS MANY DIFFERENT DISEASES

Across a variety of therapeutic areas, an increasing number of treatments are personalized, including medicines for cancer, psychological disorders, infectious diseases, and cardiac diseases, among many others.



\*FDA approvals with biomarker information in the approved labeling

Source: U.S. FDA, "Paving the Way for Personalized Medicine," Oct 2013.

# Paradigm Shift: Science, Business and Medicine

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Personalized medicine – “exquisite precision in disease diagnosis and treatment.. shift[s] the emphasis in medicine from reaction to prevention..”

- Targets populations with a greater likelihood of response to treatment and a lower incidence of side effects
- With understanding of cancer genomics, treatment is more dependent on tumor mutations than on the organ where the cancer occurs, therefore patients should be treated based on the genomic profile of their cancer, rather than the site of origin of the cancer.

[bladder cancer signatures found in lung cancer; ALK mutations in NSCLC and Hairy Cell Leukemia]

"The big vision is to bring genomic science to the bedside to better care for patients, to better diagnose their disease, better individualize their treatment, and to eventually prevent their disease in the first place." [Weinshilboum, Mayo Clinic]

*New scientific research, business strategy, physician training and medical treatment models are needed!*

# SCIENCE: Research Strategy Shift: Requires Collaboration of Pharma/Dx

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- Biomarker determination and co-development of companion diagnostics
- Regulatory alignment enabling parallel approvals
- Collaboration across industry silos
- Pharma research project planning paradigm shifts:
  - 85% of drug development research projects include “personalized healthcare strategy” [OracleHealth @ PMWC 2015]
  - Project launched in 2005 maps full molecular landscape of 20 different cancers globally to identify new molecular targets for treatment and monitoring disease progression. To date, 10 cancers completed. [ASCO]

# Growth of Personalized Medicine: “By the Numbers”

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- **Personalized Medicine Coalition data document growth in precision medications utilizing biomarkers:**
  - In 2015 there were #138 personalized medicine agents, treatments, diagnostics products available; in 2006 only #13
  - 30% of all treatments in late clinical development rely on biomarker data
  - 50% of all treatments in early clinical development rely on biomarker data
  - 60% of all treatments in preclinical development rely on biomarker data
  - 30% of all biopharmaceutical companies surveyed require all compounds in development to have a biomarker<sup>7</sup>
  - 50% of all clinical trials collect DNA from patients to aid in biomarker development
- **Trends favoring Personalized Medicine:**
  - Cost of sequencing genome down to \$1K
  - 93% of MDs use EMRs
  - #137 FDA approved meds have pharmacogenomic info in label

Source: PMC, Personalized Medicine by the Numbers, September 2015

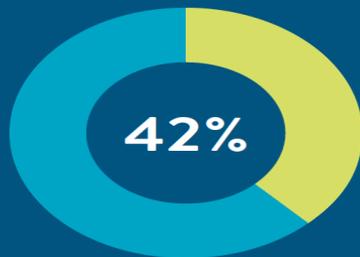
# The Pharma Industry: Shifting to Personalized Medicine

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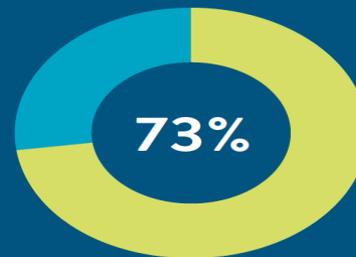
- An estimated #132 personalized medicines are currently on the market
- An estimated 42% precision medicines are in the pipeline, including 73% of cancer therapies in development

## FIGURE 7: THE BIOPHARMACEUTICAL INDUSTRY IS COMMITTED TO PERSONALIZED MEDICINE

Drug development pipelines are full of targeted treatments that offer new hope for patients.



of all drugs in  
development are  
personalized medicines



of oncology drugs  
in development are  
personalized medicines

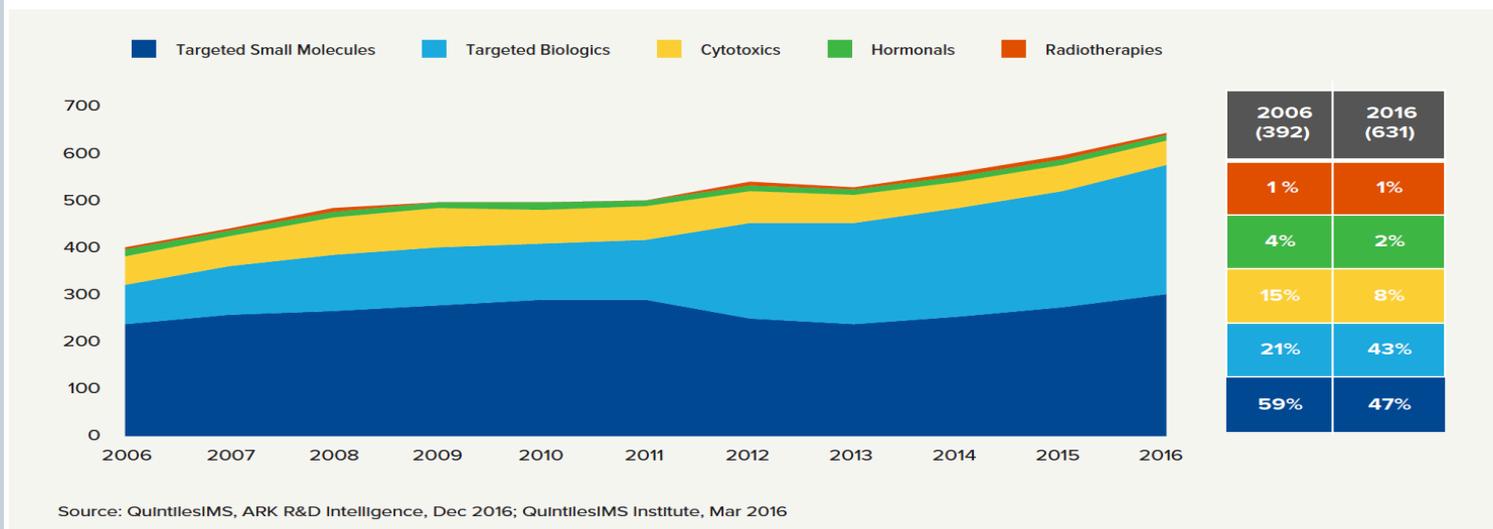
■ Personalized Medicines

# Targeted Therapeutics Comprise a Growing Proportion of Marketed and Late-Stage Portfolio Oncology Products

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*82% of new molecules launched in oncology are targeted; 90% Ph3/Reg Stage Oncology Products*

**Chart 10: Late Phase Oncology Pipeline Molecules, 2006–2016**



- 90% of the Phase 3/registration pipelines in 2016 were targeted therapies, compared to 54% in 2010.
- Targeted therapies reached 82% of all oncology new active substances launched between 2010 – 2014.
- Targeted therapy segment of oncology drugs have the highest growth, +18% CAGR from 2011-2015

# Improved CA Survival Rates with Targeted Meds

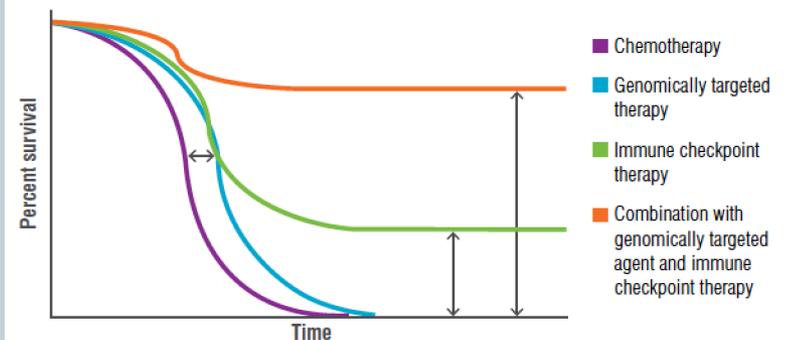
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- Advances in oncology therapy show opportunity to turn fatal disease into chronic, treatable condition
- Analysis of tumor genetics leveraged into customized lab tests
- Genomic “Pre-profiling” identifies biomarker-defined oncology patients for clinical trials, enabling cost effective drug development and treatment
- Molecular characterizations of clinical samples are used for cell therapies, cancer-specific vaccines, and immunotherapies

**Table 1: Response rates, toxicity and long-term survival with various oncology therapies**

Therapy	Response rate	Toxicity	Long-term survival
Chemotherapy/radiation	Low	High	Poor
Targeted therapy	High	Low	Moderate
Immunotherapy	Mid	Low	Good

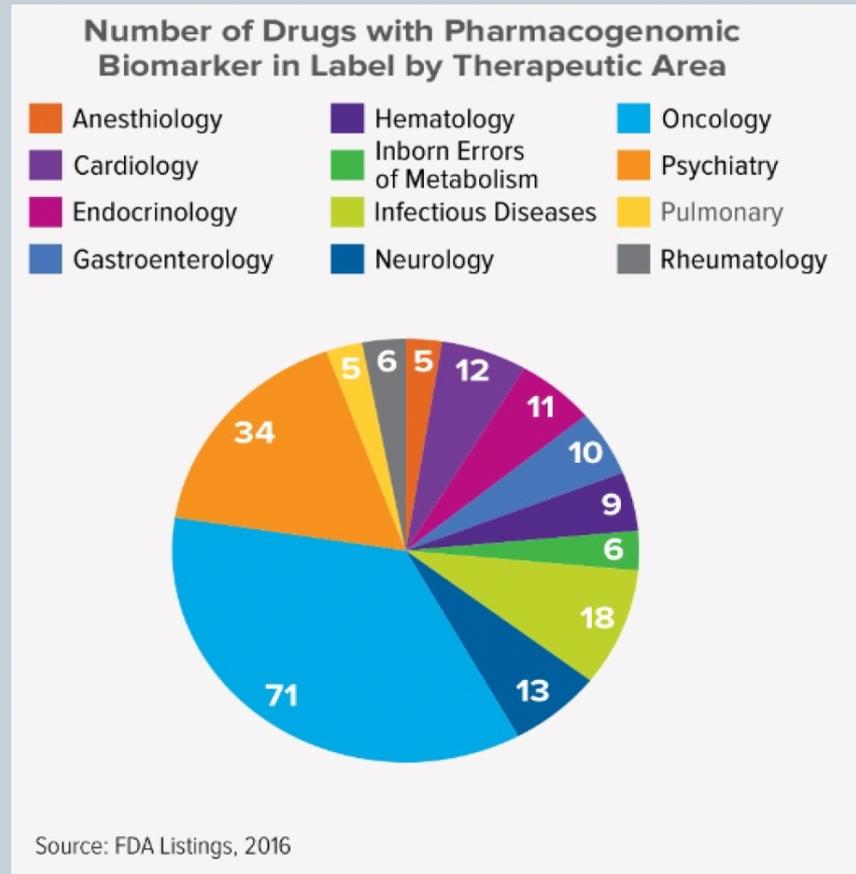
**Figure 2: Survival rates for various cancer therapies<sup>6</sup>**



# Currently 200 Marketed Medications with Associated Biomarker/Genetic Element

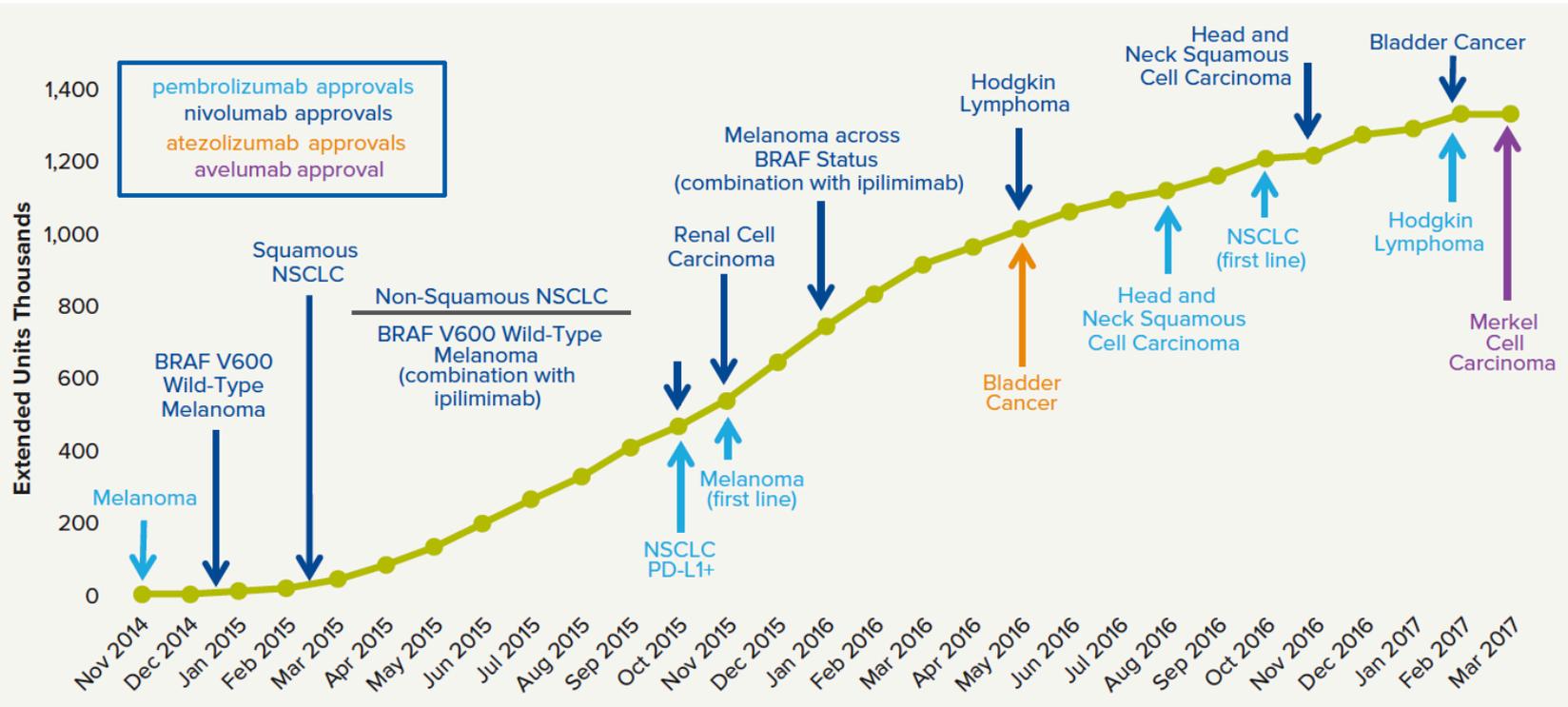
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- 71 of these medications oncology-related



# Rapid Uptake Immuno-Oncology Agents

Chart 4: Immuno-Oncology PD-1 and PD-L1 Inhibitor Uptake in the United States



Source: U.S. FDA, QuintilesIMS, National Sales Perspectives, Feb 2017; QuintilesIMS Institute, Apr 2017

# Oncology Highest Potential for Precision Medicine Uses

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- McKinsey maps potential in therapy areas: Next Frontier: Immune-related, pediatric/pre-natal, infectious disease
- CNS and CV in early stages but high potential

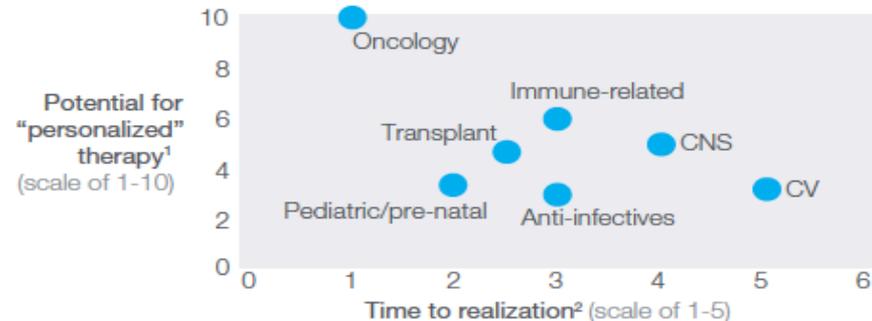
*Oncology will continue to be the leading “playground” for personalized medicine with new understanding of disease and new Dx technologies*

*In the near term (3 to 5 years), the next frontier of personalized medicine is likely to be in immune-related, pediatrics/pre-natal, and infectious diseases*

*In the long-run, CNS and cardiovascular have tremendous potential for personalized medicine, but still in early stages of development*

FIGURE 2

## Potential for personalized medicine across disease areas



<sup>1</sup> Potential based on understanding of disease heterogeneity, clinical relevance of personalized Dx and economic attractiveness

<sup>2</sup> Years to realization based on disease understanding, technical feasibility and development timeline for therapeutics

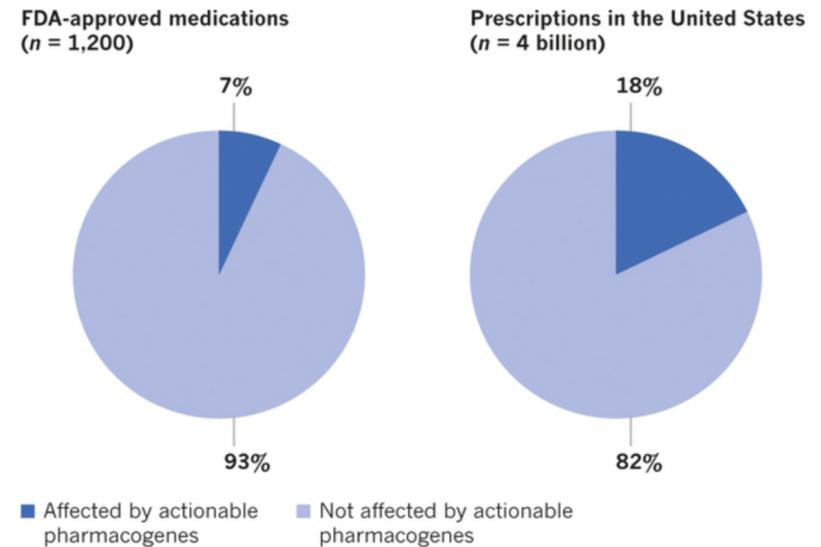
<sup>1</sup> *The Microeconomics of personalized medicine: today's challenges and tomorrow's promise*, accessed at <http://www.nature.com/nrd/journal/v8/n4/full/nrd2825.html>

# Precision Medicine Integrates Research with Clinical Practice

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- Nature Supplement Oct 2015 dedicated to Precision Medicine *Insight* examines current progress in pharmacogenomics, gene therapy, and genomics in target validation approaches
- Sharing data is essential: U.S. 1 million patient Precision Medicine Initiative; UK 100,000 Genomes Project
- Currently 7% of FDA approved meds have “actionable pharmacogene” info in the PI; 18% of U.S. Rx’s
- Future clinical trials for oncology drugs would be optimized if utilize a tumor-specific “consortium approach” to target patient population for optimal studies
- Implementing genetic testing processes into physician practices will require a new workflow: identifying the gene, assess potential treatments, develop clinical guidelines, monitor treatment, analyze cost benefits; audit the impact

Figure 2: Medications affected by actionable pharmacogenes.



Approximately 7% of FDA-approved medications are affected by actionable inherited pharmacogenes (left), and approximately 18% of US outpatient prescriptions are affected by actionable germline pharmacogenomics (right)<sup>45</sup>, which demonstrates that several pharmacogenetically high-risk drugs are commonly prescribed.

# Patient Disease Gene Mining: Pharma Partnering with 23andMe

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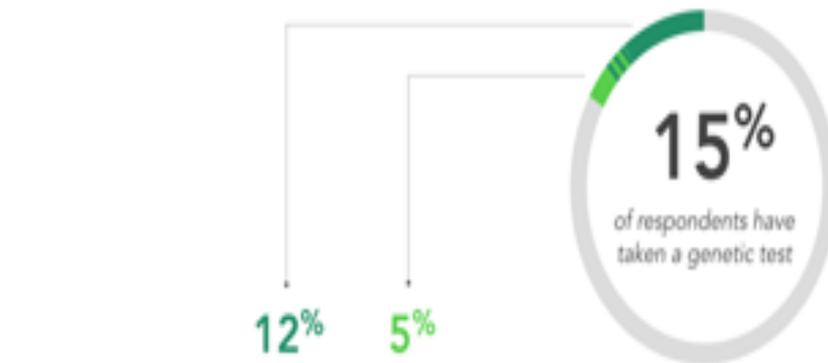
- Pharma companies are utilizing commercial genetic data resources such as 23andMe to identify patients who have or are likely to have a range of diseases and to identify precision drug targets
  - Genentech/Roche and Pfizer are partnering with 23andMe to identify the genes responsible for Parkinson's [Genentech] and IBD: Ulcerative Colitis and Chron's Disease [Pfizer]
- 23andMe's database now has 2 million genotyped participants available for conduct virtual studies of diseases, identify disease targets, and select patients with disease/genetic targets for clinical trials
  - Major universities and Pharma are collaborators

# Patient Adoption of Genetic Testing

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## GENOMICS ADOPTION

Percentage of adoption by channel

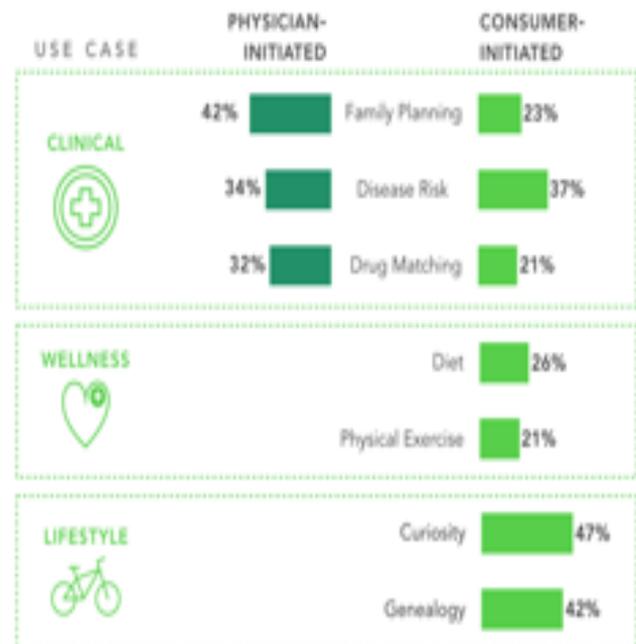


SURVEY		PHYSICIAN-INITIATED	CONSUMER-INITIATED
18%	% 25-34 y/o	49%	37%
53%	% high income	87%	82%
67%	% "healthy"	40%	46%
52%	% female	28%	21%
93%	% insured	98%	96%

## REASONS FOR TAKING

Percentage indicating reason

ROCK  
HEALTH



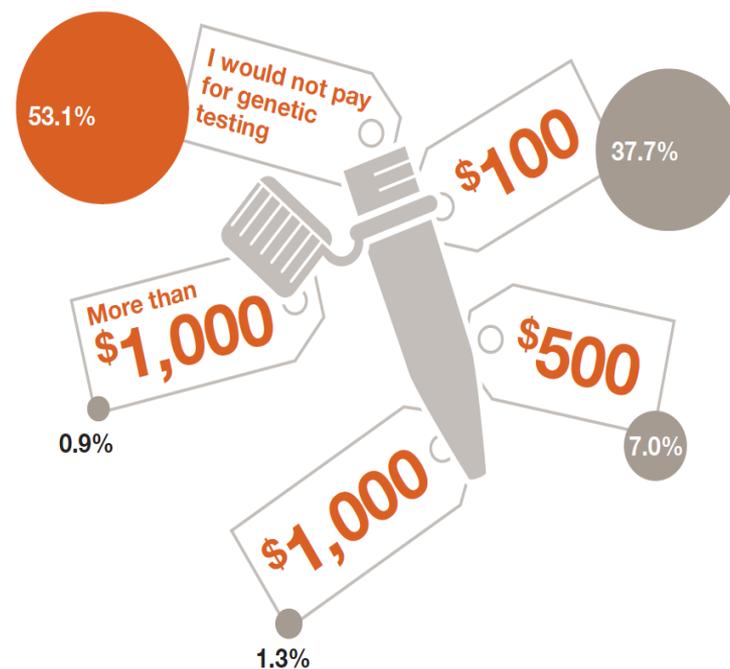
# The Business Case for Personalized Medicine: Cost Effectiveness and Patient Needs

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- Payers will require evidence beyond safety and efficacy data from clinical trials:
  - Pharma needs in addition to utilize EHRs, genomics economic data, and labor statistics to communicate value [PwC 2014]
- Non-responders in some diseases greater than 50%
  - value in predicting response/reducing wastage of drugs on non-responders [McKinsey 2014]
- Half of patients would pay more for personalized medical products
  - are divided on willingness to pay for the enabling tests. [PwC]

**Figure 6: Most US consumers are unwilling to spend much for genetic testing**

Amount US consumers are willing to pay for genetic testing



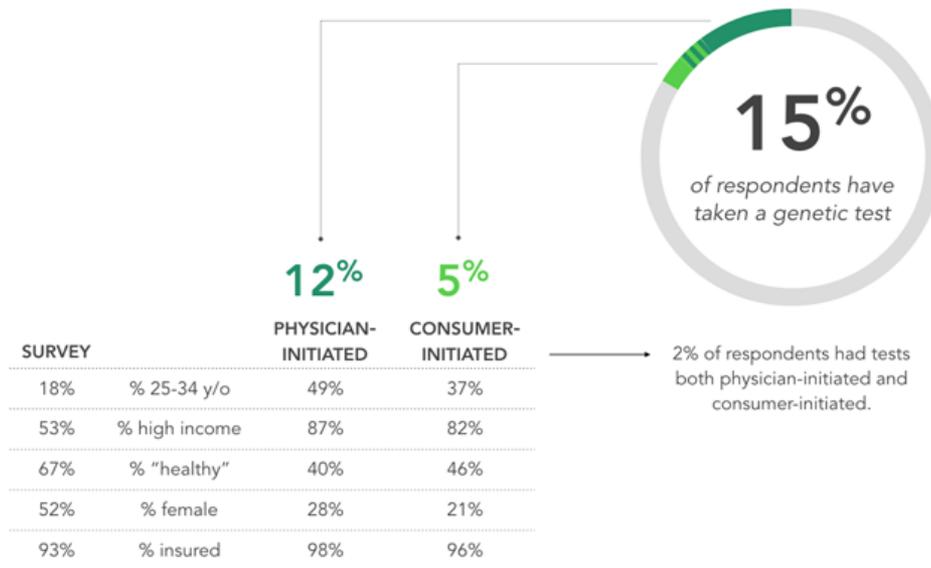
Sources: HRI Consumer Survey, PwC, 2014

# Genomics Adoption in U.S. population: Only 15% have taken a genetic test 2016

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## GENOMICS ADOPTION

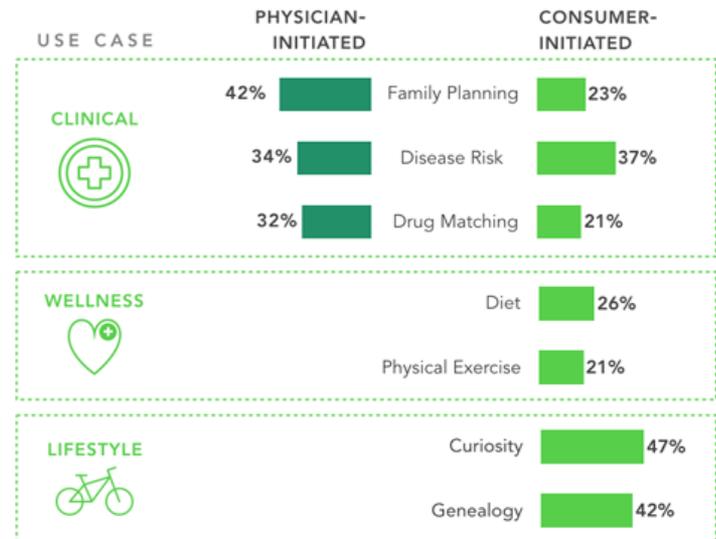
Percentage of adoption by channel



## REASONS FOR TAKING

Percentage indicating reason

**ROCK  
HEALTH**



# Medical Treatment Will Be Disrupted:

## Lack of Training for MDs a Major Hindrance, but Patients will be Drivers

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- Majority of practicing physicians don't fully understand genetic test results and aren't able to take time to discuss options with their patients [survey in *Genetics in Medicine* via @ New Yorker, February 2015]
  - MedSeq project at Harvard trains MDs/recruits patients for genome sequencing and optimizes doctor/patient interactions [@NewYorker]
  - Fast pace of genetics research, variability of test methods and “aura of infallibility” of results contribute to complexity for practicing clinicians [@NewYorker]
  - New genomics counseling specialty recommended [@SNPgenomics]
- Management of patient is changed in 50% of the cases when genetic testing is utilized [@SNPgenomics]
- In one in five advanced cancer patients, DNA testing was able to identify specific treatments that slowed the progress of the cancer [Economist, January 2017]
- Need “clinical grade whole genome sequence”
  - 4 P's Predictive, preventive, personalized and participatory [Hood's vision was quoted @ PMWC 2015]
- Applying John Scully's “rise of consumerism” in book ‘Moonshot’ to personalized medicine
  - “exponential growth of big data, cloud computing, mobile devices, and ultimately the internet of things is creating a market power shift from traditional producers who are in control of businesses to customers. Big data is making customers smarter and customers, now, are paying more attention to what other customers have to say.” [Scully in Forbes]

# Precision Medicine: Partnering w/Government

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President Obama's 1 million person, \$215 million Precision Medicine initiative: implementation options described by Collins and Varmus in NEJM 2015, plans finalized by PMI Working Group in September 2015; July 2016 announcement by NIH of 5 centers coordinating November 2016 recruitment

- Near-term portion of initiative focus on cancer
  - Analysis of “many more” cancer genomes, clinical trials with novel designs, and “more reliable” models for preclinical testing as well as a “cancer knowledge network” to store and share info
- Longer-term focus on other diseases
  - Application toward inherited diseases, infectious diseases, immune disorders

Assemble a cohort of 1+ million U.S. participant genomes and data

- Columbia, Northwest, University Pittsburgh, University Arizona
- Dr. Eric Topol of Scripps will work with Walgreens, Apple, Blue Cross, Verizon, and other companies on notifications and apps and develop wearables to track health data for the initiative

Align regulatory frameworks to enable sharing of data

10 year timeline outlined by PMI Working Group report: initial risk factors, pharmacogenomics and biomarker discovery; over time mHealth connections

*Benefits expected in cancer treatment, pharmacogenomics, new drug targets, and use of mobile technology to improve prevention and treatment of chronic diseases.*

# 1 Million Patients to Participate in U.S. Precision Medicine Initiative

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- Public-private partnership with NIH and more than 50 companies to build nationwide million-person cohort of patients
- Goal to study genomic differences across a diverse patient pool
- Pharma companies, universities, tech companies all involved
- Online survey of Americans show support for the initiative, however just 14% would “definitely” participate and 40% “probably” would”

# NCI- MATCH Molecular Tumor Study

## ~5,000 Patients

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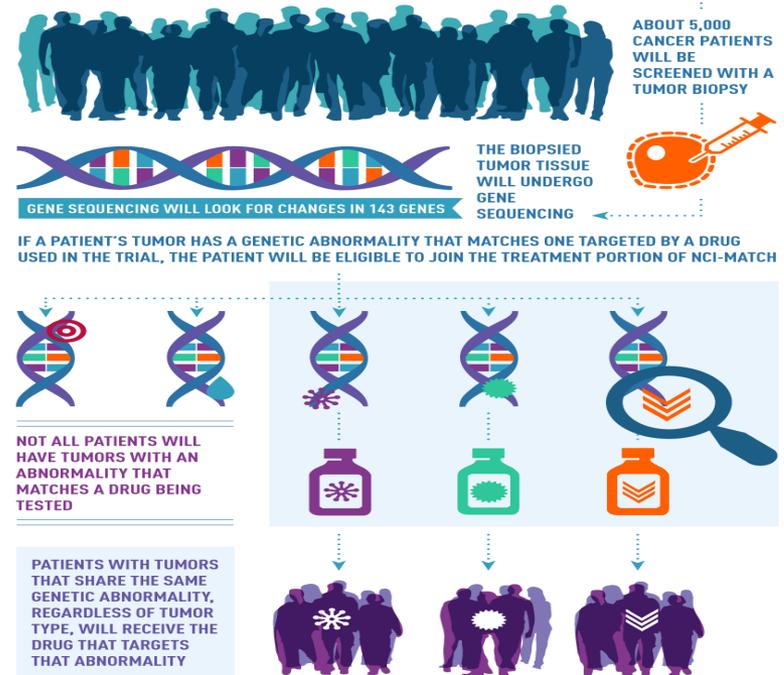
- Clinical trial program identifying actionable tumor mutations in solid tumors and lymphomas, initiated in August 2015
- Tumor biopsy specimens are analyzed by DNA sequencing for 4,000+ different variants, across 143 genes.
- Patients are identified and 'matched' to marketed and/or research treatments which target the tumor genetic abnormalities.
- If agent not effective, patients are eligible for an alternative Match

### NATIONAL CANCER INSTITUTE NCI-MATCH CLINICAL TRIAL

THIS PRECISION MEDICINE TRIAL EXPLORES TREATING PATIENTS BASED ON THE MOLECULAR PROFILES OF THEIR TUMORS

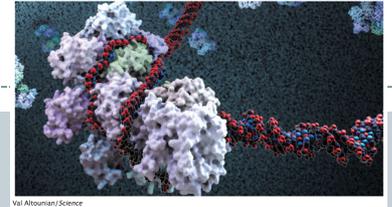
#### NCI-MATCH\* IS FOR ADULTS WITH:

- solid tumors (including rare tumors) and lymphomas
- tumors that no longer respond to standard treatment



# Genetics will Power New Research Methods and Potential for Cures

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- Gene editing research is showing promise
  - CRISPR-Cas9 is a programmable protein discovered by CAL Berkeley scientist Jennifer Doudna, used as a “genetic scalpel” to “slice DNA”
  - Many potential uses in research: animal models
    - ✦ Engineering animals to develop human disorders and then test agents to treat the disorders
    - ✦ Speeds research, cuts time from a year to several weeks to develop animal models with ie the autism-related gene
- First human studies likely for single gene defect blood disorders such as sickle cell
- Ethics of gene editing, especially in embryos, being debated by experts

# Hospitals Re-Invented: New Facilities Embed Precision Medicine

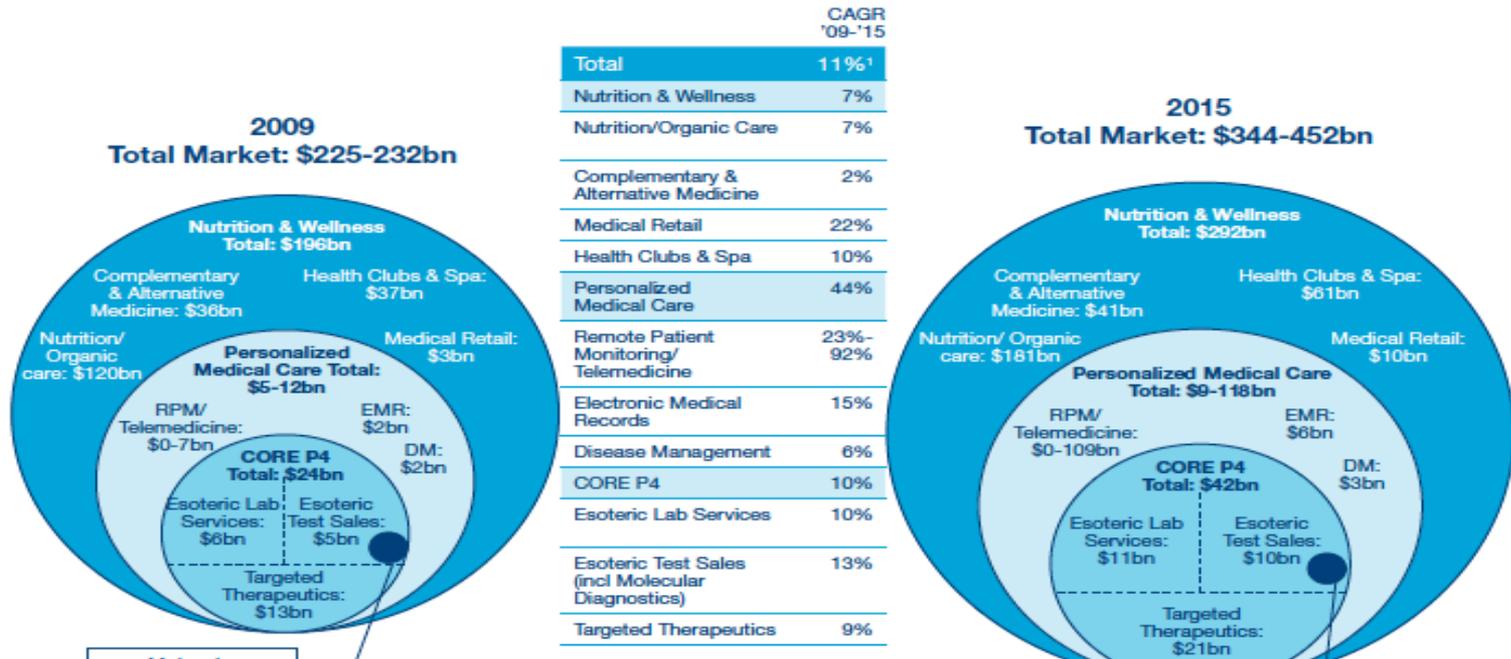
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- New UCSF Mission Bay's focus on Precision Med
  - “finalizing university's vision to provide more personalized patient care...
  - create a closer relationship between its physicians at the hospital and its scientists conducting biomedical research.”
- “Linking clinical care with research ....will translate ideas into practice more quickly and turn discoveries into treatments and cures targeted specifically for a patient's biology”

# Personalized Market Estimated Growth 2009-2015

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## Personalized Medicine Market Size, 2009 and 2015



Note: Totals may differ due to rounding  
<sup>1</sup> Reflects upper range of RPM/Telemedicine  
 Source: PricewaterhouseCoopers analysis.

A broader definition of the market could include:

- Stem cell products growing from \$2bn in 2009 to \$3-21bn in 2015
- Genetically Modified products growing from \$5bn in 2009 to \$20bn in 2015

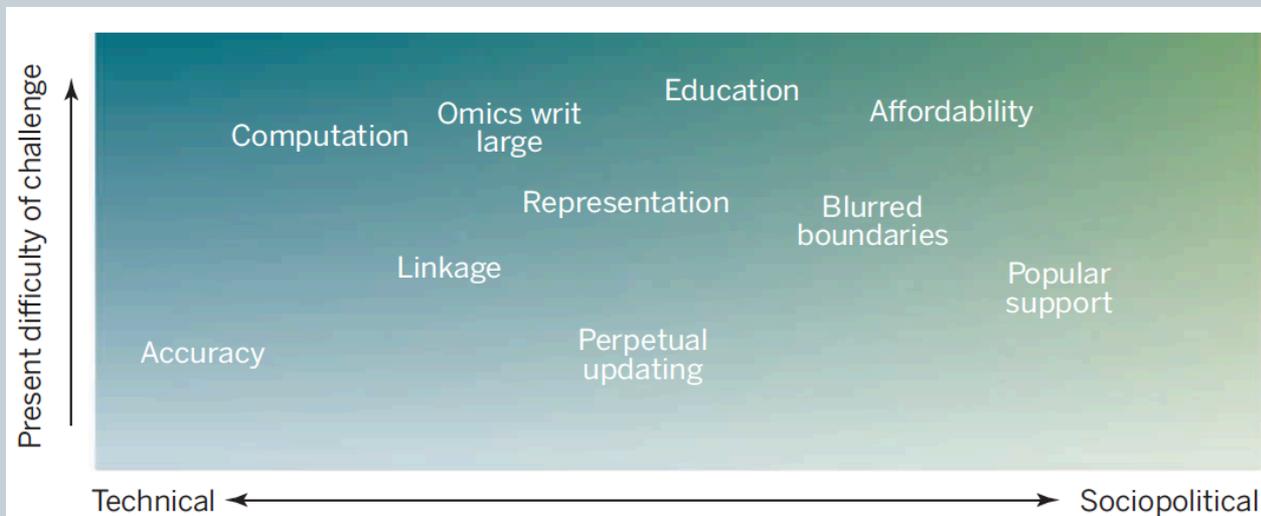
PricewaterhouseCoopers defines personalized medicine more broadly, as products and services that leverage the science of genomics and proteomics (directly or indirectly) and capitalize on the trends toward wellness and consumerism to enable tailored approaches to prevention and care.

Source: PwC The New Science of Personalized Medicine 2009

# Key Hurdles to Achieve Precision Medicine

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*“The combination of clinical findings and genomic sequencing is already resulting in life-saving cancer treatments...with more precise molecular characterizations of outcomes over time within populations, selection of primary prevention regimens can become more data driven, and unwanted effects could be minimized... [Ten] surmountable challenges will have to be addressed to realize its full potential” Isaac S. Kohane*



**Moving toward precision medicine.** Ten challenges for achieving precision medicine are qualitatively ordered on the x axis by how much they are intrinsically technical versus sociopolitical challenges. The y axis qualitatively orders the difficulty each challenge currently presents if we are to attain the widely articulated goals for precision medicine.

# Drivers and Challenges for Personalized Med

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## Advantages for adoption of personalized medicine: [Source: PMC 2014]

- Shift from reaction to prevention
- Reduce trial-and-error prescribing
- Avoid adverse drug reactions
- Increase patient compliance
- Improve quality of life
- Reveal additional uses for medicines
- Payers mandating Dx/cost control

## Drivers: [McKinsey 2013]

- Payers mandating Dx for proper use
- Heterogeneity disease/safety signals
- Improvement technology & Dx testing
- MD interest in more info
- Informed & active consumers
- Digital, mobile, IT technology advances

## Challenges for routine use in clinical practice [Source: FDA 2013]

- Limited understanding of the intrinsic biology of disease:
- Common conditions involving multiple genes/biomarkers:
- An outdated disease classification system:
- Lack of infrastructure:
- Clinical implementation of new diagnostics:
- Investment uncertainties:
- Access to personalized therapeutics

# Breakthroughs in the Next Decade

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- Cancer Stem Cells
- Faster, cheaper, complex genomic analytics, genome editing
- Liquid biopsies of circulating tumor DNA and RNA
- Nanomedicine
- Utilization of Big Data Tools/Health IT
  - a new class of data/IT “players” will emerge to capture value – developing solutions for Dx data interpretation, clinical decision support and analytics for R&D [McKinsey]

# The Future: Transformative

“Do-it-Yourself Healthcare” and “Mobile App to Medical Device”

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- Consumers and MD's are ready to “embrace a dramatic expansion of the personal medical kit in 2015”
  - Technical innovation/wearable tech
  - Public's craving for convenience
  - Push to lower-cost care
- 90% of MDs say that mobile & wearable devices will be important to their practices in the next 5 yrs
  - Example: 1/5 consumers would use a home urinalysis device/  
1/2 of MD's would use data from the device to Rx or recommend visit

# Digital Medicine will Provide Personalized Care

- According to McKinsey's August 2015 report, in the next 5 to 7 years, Pharma companies will market products that are “part of a digital ecosystem that constantly monitors a patient's condition and provides feedback to the patient and other stakeholders”
- An example is for Parkinson's monitoring and treatment:
  - “Parkinson's patient might include a medication regimen with “chip on a pill” technology to monitor drug taking along with a smartwatch that monitors the patient's condition,
  - sends him or her reminders to adhere to the prescribed treatment, sends the neurologist compliance and health-status reports.
  - The neurologist can then coach patients on lifestyle changes or even customize therapy remotely.” [McKinsey]
- “Such digitally enabled approaches to patient care are likely to improve outcomes to the extent that they could become a condition of reimbursement, particularly for expensive specialty drugs.”

# The Future of Medicine: In the Hands of the Patient

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## Eric Topol's "The Patient will See You Now"

- predicts that new technology – from the smartphone to machine learning – will “democratize” medicine.
- Patients will control their data
- Smartphones enable a range of medical applications “shifting locus of control from doctor to patient”
  - Physiological data via smartphone as ‘point of care’ device
  - Sequence genome/detect cancer molecules in your breath
  - Implanted sensors in tissues and in wearables

Transformational Power of Patient Data and Analytics will  
Contribute to Successes in Precision Medicine

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