Building Consortia for Enhanced Predictive, Diagnostic, and Therapeutic Care: The Example of the Biomarkers Consortium

Best Practices for Personalized Medicine
Vancouver, BC
March 9, 2011

Building Consortia for Enhanced Predictive, Diagnostic, and Therapeutic Care

- *The ultimate deliverable:translation of personalized medicine to the clinic and patient*

  Dr. Daniel Bednarik, Director, Genomics and Bioinformatics, Cardiome Pharma

- *Strategies and barriers to deliver personalization to the point of care*

  Dr Brad Popovich, Chief Scientific Officer, Genome BC

- *ASK for confident decisions: harnessing the power of semantics*

  Dr. Erich Gombocz, Vice-President and Chief Scientific Officer, IO Informatics

Convergence of multiple factors has led to the emergence of public-private partnerships in biomedicine

THE biomarkers CONSORTIUM

Escalating complexity of biomedical science and technologies

Declining productivity in biopharma R&D → "externalization" of research

Decline in government health research budgets → funding gap

Increased Need for Public- Private Partnerships

Regulatory challenges → increasing complexity, limited budgets

Emergence of viable collaborative models → e.g., SNP Consortium, Gates Foundation

Expansion of "pre-competitive" field

Biomarkers have many uses

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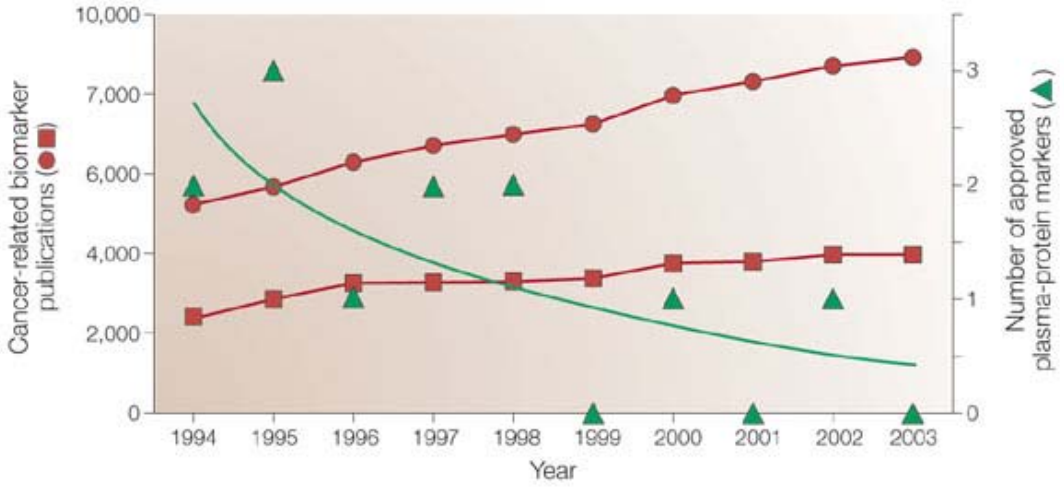
Personalization

- Clinical Practice
  - Diagnose or identify risk for disease
  - Stratify patients
  - Assess severity/disease progression
  - Predict prognosis
  - Guide treatment
  - Assess response to treatment
- Drug Development
  - Assess role of drug target in disease process
  - Assess how a drug candidate interacts with a target receptor, enzyme, or protein
  - Toxicology – PK, PD, dosing
  - In clinical development, assessing whether a drug is safe and effective
- Drug Qualification
  - Inform regulatory decision-making

Out of 1,261 putative cancer protein or peptide biomarkers described in the literature*, only 9 are FDA approved as “tumor associated antigens”

- Fewer than 1 per year have been approved by the FDA since 1998
- This high percentage of un-validated biomarkers is generalizable to other diseases
- This “biomarker barrier” in which candidate biomarkers have not been validated needs to be overcome



** Polanski and Anderson (2006). A List of Candidate Cancer Biomarkers for Targeted Proteomics. Biomarker Insights 2:1– 48*

Biomarker qualification: the value of collaboration

- Biomarkers require extensive testing and qualification for practical use
  - Multiple studies to ensure integrity, reproducibility of results
- Qualification is challenging, expensive, and time-consuming
  - Can require large amounts of data: literature, observational studies, clinical trials
- Qualification is based on *consensus* among the scientific community
  - Deep understanding of and agreement on disease risk, natural history, outcomes
- Qualification is a pre-competitive activity
- Qualification is difficult to accomplish this in a single institutional setting

→ Requires *partnerships* and a *strategic approach*

As a result, a number of PPPs in biomarker discovery and development have emerged in recent years

Some examples:

- ADNI
- Critical Path Institute (PSTC, CAMD)
- Serious Adverse Events Consortium
- Innovative Medicines Initiative (Europe)
- PROOF Centre
- The Biomarkers Consortium

Foundation for NIH Overview

- Established by Congress in 1990; incorporated in 1996

- Supports the NIH mission
- Close relationships with NIH

- 501(c)(3) non-profit organization
  - Raised over $560M since 1996
  - 50+ projects

- Non-governmental
  - Directly solicits contributions
  - Flexible donor relationships
  - Creates open, inclusive, objective governance mechanisms
  - Timely, effective grants/contracts/project management

Goals of The Biomarkers Consortium

- Facilitate the development and standardization of biomarkers using new and existing technologies
- Help qualify these biomarkers for specific applications in diagnosing disease, predicting therapeutic response, or improving clinical practice
- Generate information useful to inform regulatory decision-making
- Make consortium project results broadly available to the entire scientific community

Contributing Members (62)

THE biomarkers CONSORTIUM

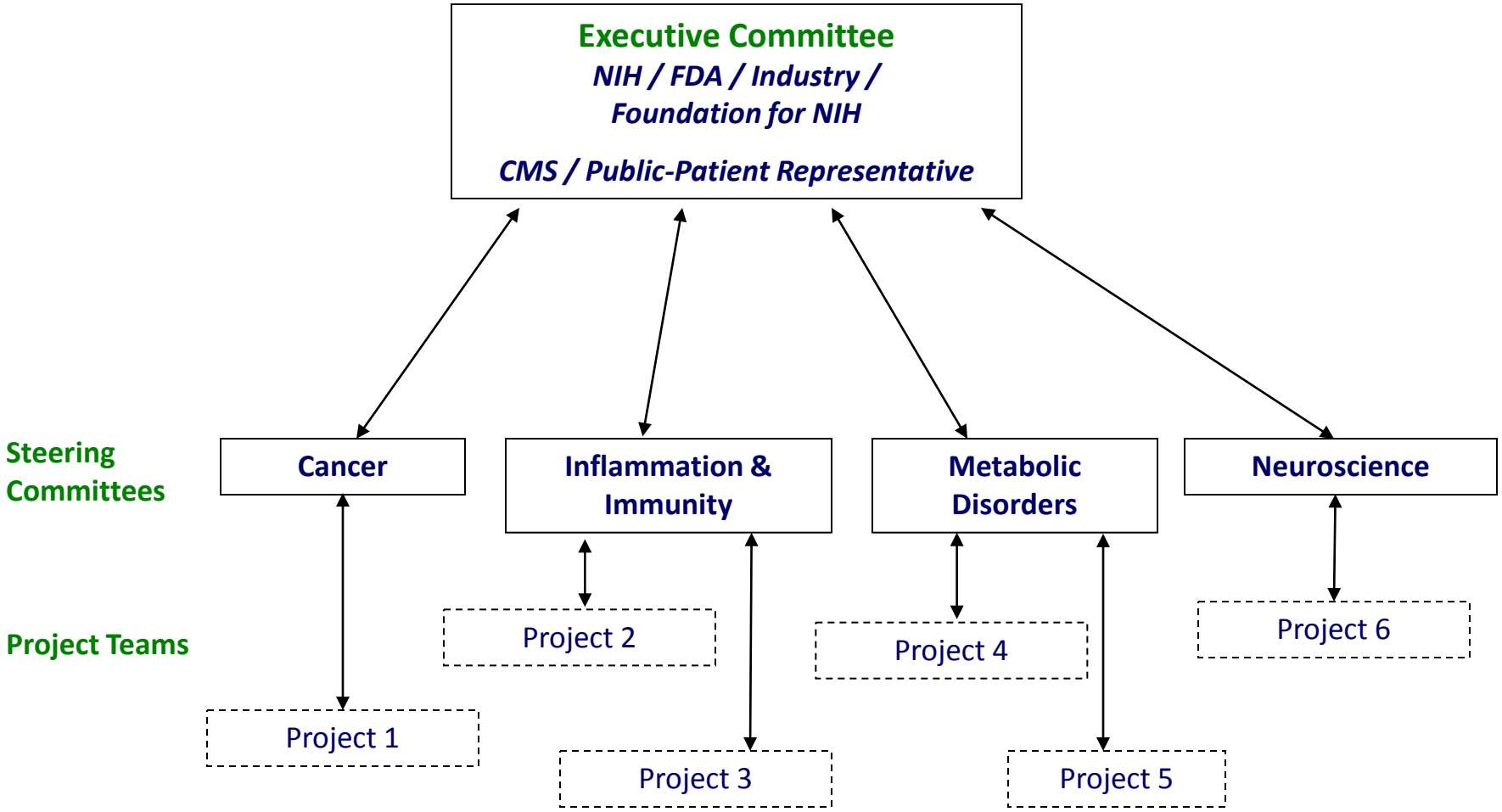
For-Profit Companies (28)

Abbott Laboratories
Amgen
Amylin
AstraZeneca
Banyan Biomarkers
BG Medicine
Boehringer-Ingelheim
Bristol-Myers Squibb
Celgene Corporation
Daiichi Sankyo
Eisai, Inc.
Genstruct, Inc.
GlaxoSmithKline
InfraReDx, Inc.
Johnson & Johnson
Eli Lilly and Company
Merck and Co., Inc.
Meso Scale Discovery
Metabolon, Inc.
NextGen Sciences
Orasi Medical, Inc.
Pfizer Inc.
F. Hoffmann-La Roche
RareCyte, Inc.
Scout Diagnostics
Sepracor
Takeda Pharmaceuticals
XOMA, Ltd.

Non-Profit Organizations (34)

Academy of Molecular Imaging
Advanced Medical Technology Association
Alliance for Aging Research
Alzheimer's Association
American Association for Cancer Research
American College of Neuropsychopharmacology
American Diabetes Association
American Health Assistance Foundation
American Society of Clinical Oncology
American Society for Clinical Pharmacology and Therapeutics
American Society for Therapeutic Radiology and Oncology
Arthritis Foundation
Association of Clinical Research Organizations
Autism Speaks
Avon Foundation
Battelle Memorial Institute
Biotechnology Industry Organization
CHDI Foundation
Cystic Fibrosis Foundation Therapeutics
Federation of Clinical Immunology Societies
The Hamner Institutes for Health Sciences
The Immune Tolerance Institute, Inc.
International Society of Biological Therapy of Cancer
Juvenile Diabetes Research Foundation
Kidney Cancer Association
The Leukemia and Lymphoma Society
Michael J. Fox Foundation for Parkinson's Research
Ontario Cancer Biomarker Network
Osteoarthritis Research Society International
Pharmaceutical Research and Manufacturers of America
PROOF Centre of Excellence
Radiological Society of North America
Society for Nuclear Medicine
University of Illinois

Governance


Executive Committee
NIH / FDA / Industry / Foundation for NIH
CMS / Public-Patient Representative
Steering Committees
Cancer
Inflammation & Immunity
Metabolic Disorders
Neuroscience
Project Teams
Project 1
Project 2
Project 3
Project 4
Project 5
Project 6

The Biomarkers Consortium Executive Committee

THE biomarkers CONSORTIUM

Chairman
Charles Sanders, Foundation for NIH

NIH
Thomas Insel, *National Institute of Mental Health*
Douglas Lowy, *National Cancer Institute*
James Battey, *National Institute on Deafness and Other Communication Disorders*

CMS
Barry Straube

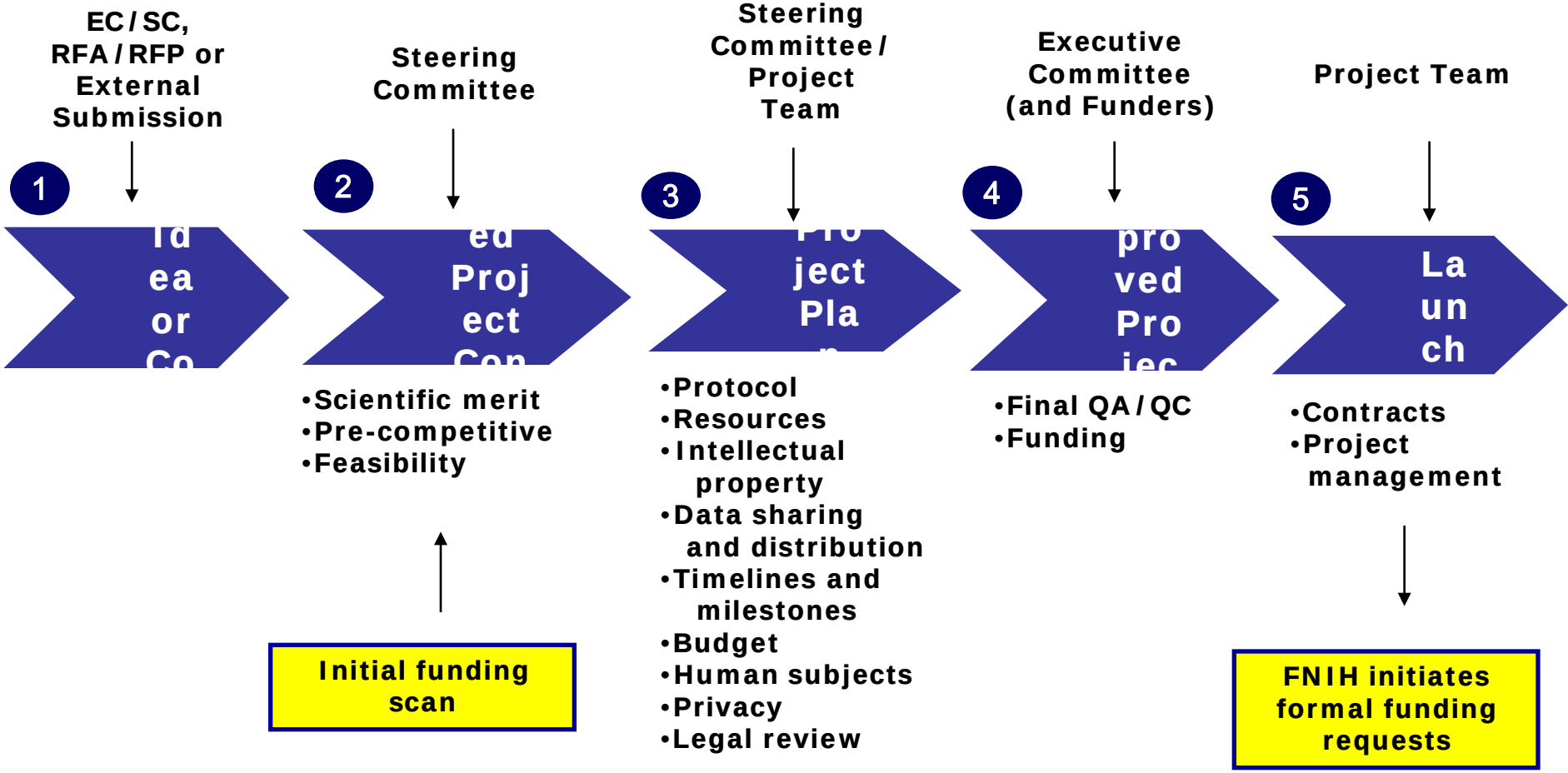
Public Member
Mary Woolley, *Research!America*

FDA
ShaAvhree Buckman, *Office of Translational Science*
Jeffrey Shuren, *Center for Devices and Radiological Health*
Janet Woodcock, *Center for Drug Evaluation and Research*

Industry
Stephen Eck, Eli Lilly & Co.
Gary Herman, Merck & Co., Inc.
Garry Neil, Johnson & Johnson
Sara Radcliffe, BIO

Foundation for NIH Board
Steve Paul, ex-Eli Lilly & Co.
Ellen Sigal, Friends of Cancer Research

Project Development Process

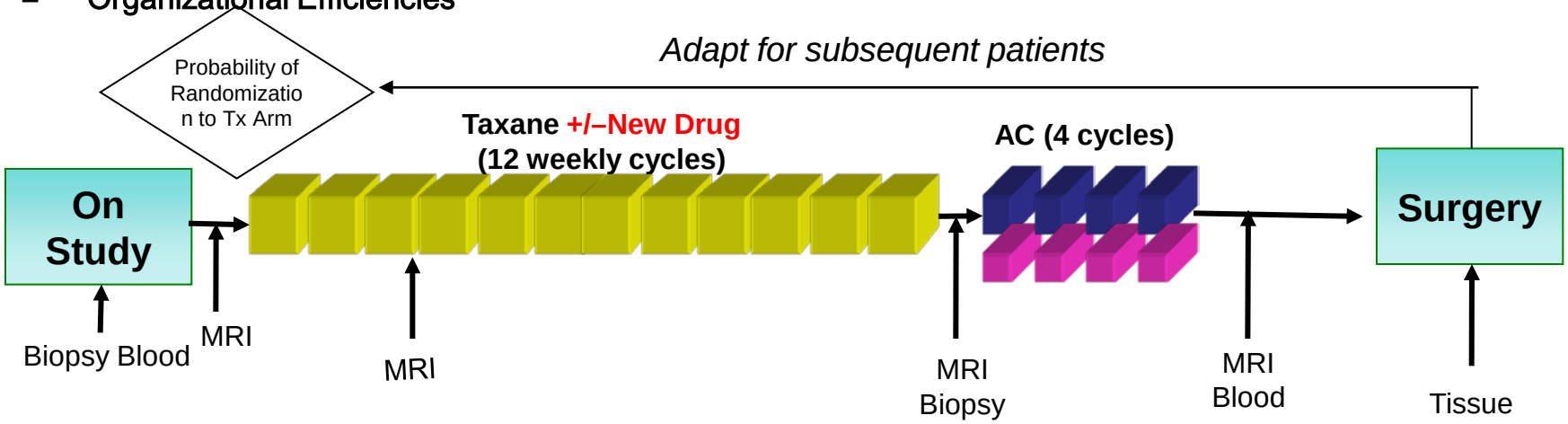


Accomplishments to Date

- 11 launched projects (1 completed)
  - 1 completed project (Adiponectin); 4 projects will complete in 2011
  - 3 new projects in 2011 pipeline (infectious disease, OA, atherosclerosis)
- Trending towards more industry- and FDA-based submissions, more qualification projects
- Increased membership base/operations core
- Increasingly seen as a model public-private partnership

I-SPY 2 is Designed to Accelerate the Clinical Trial Process

- **Neoadjuvant Setting**
  - Chemotherapy before surgery in a population with locally advanced breast cancer (LABC)
  - Accelerates knowledge turns from 5+ years to 1 year
- **Adaptive Trial Design**
  - Learn rapidly which drugs work for which patients, and apply that knowledge to subsequent patients within the trial
- **Molecular and Imaging Biomarker Guidance, and qualification of new biomarkers**
- **Multiple Drugs Tested Simultaneously, representing different signaling pathways**
- **Organizational Efficiencies**



I-SPY 2 Project will allow faster development of better targeted treatments for breast cancer:

- Dramatically improve the success rate for Phase III trials, from 25- 30% historically to as high as 85% , and target therapies to patients where the benefit is greatest
- Significantly reduce the time to identify the best compounds and move them to approval
- Reduce the number of patients required in Phase III trials tenfold (from thousands to hundreds of patients)
- Significantly cut the cost of late-phase drug development (by reducing the time and number of patients required in trials)
- Test new, more efficient paradigms for drug evaluation and approval in concert with FDA

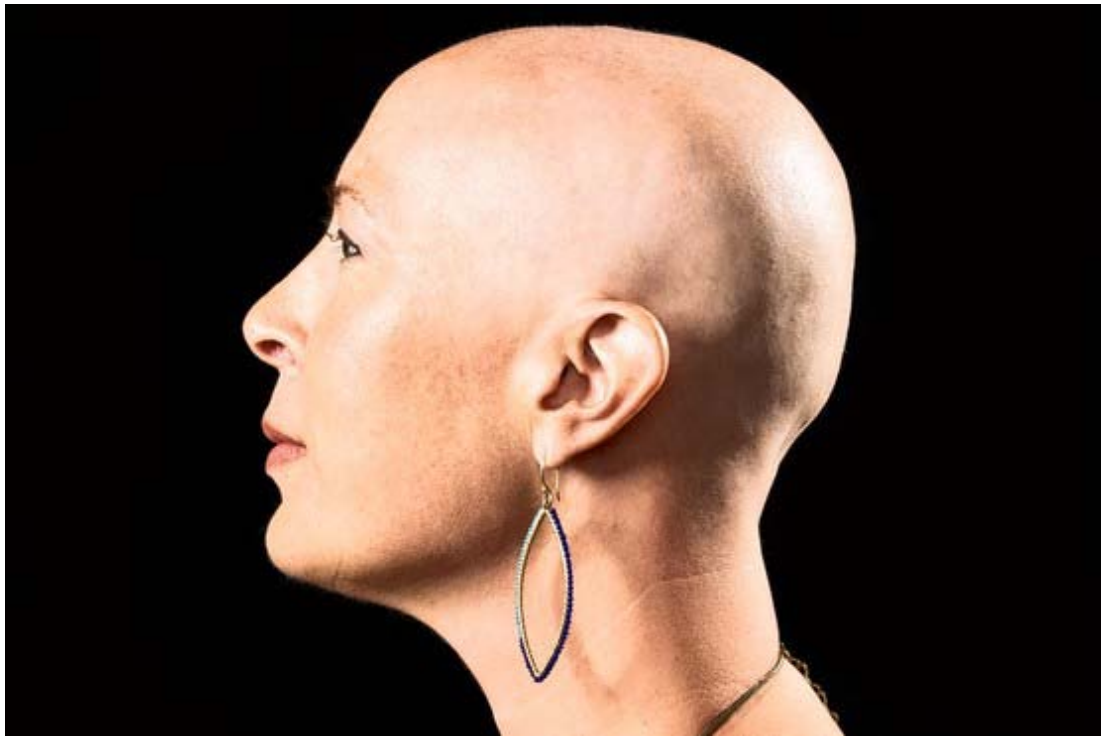
THE WALL STREET JOURNAL.
WSJ.com

THE SATURDAY ESSAY | OCTOBER 2, 2010

A New Rx for Medicine

Fed up with slow drug trials, cancer patients and doctors are testing a fast track to personalized treatments.

By RON WINSLOW



When 37-year-old Kerry Landreth discovered a lump in her breast last April, she was told it would take three weeks to get a doctor's appointment to have it checked.

"I don't do three weeks," she recalls saying. "How about today?"

By the end of the day, she had talked her way into a doctor's appointment, a mammogram and a biopsy to determine whether the suspicious lump was a tumor. A few days later came the diagnosis: stage 2 invasive ductal breast cancer, a particularly aggressive form of the disease. When a surgeon recommended a double mastectomy, she decided to consider other options.

Thank You

Definition of a Biomarker

"A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention"

(*Biomarkers Definitions Working Group, "Biomarkers and surrogate endpoints: Preferred definitions and conceptual framework," Clinical Pharmacology & Therapeutics, 69 (3): 89-95 (March 2001).*

Projects Launched/Completed to Date (11)

Project Name/Committee	Execution Objective	Status
FDG-PET Lung and Lymphoma Projects (Cancer SC) [2 projects]	Build case for FDA incorporation of FDG-PET into outcome measures for lung cancer/lymphoma	Launched 1-2Q/2007; five year projects
I-SPY TRIAL 2 (Cancer SC)	A personalized medicine trial that promises to accelerate the pace of identifying effective novel agents for breast cancer; patients will be classified according to biomarker profiles and randomized to control therapy for up to 12 agents	Approved for execution Q3 2009 (9/2009); press conference announcing launch in March 2010
Adiponectin Project (Metabolic Disorders SC)	Determine whether adiponectin has utility as a predictive biomarker of glycemic control	**Completed project** – publications released in June 2009
Carotid MRI Reproducibility Project (Metabolic Disorders SC)	Establish a standardized carotid MRI protocol and impact of site/platform on reproducibility	Launched Q3 2008; 24 month project
Sarcopenia Consensus Summit (Metabolic Disorders SC)	Generate a consensus definition of sarcopenia (age-related decrease in skeletal muscle mass) to provide specific guidelines for diagnosis/better enable regulatory decisions	First phase launched July 2009; two year project
Identification and Validation of Markers that Predict Long-Term Beta Cell Function and Mass (Metabolic Disorders SC)	Methodologic studies of the Meal Tolerance and the Maximum Stimulation Tests to validate and extend published data, as a prerequisite for a clinical trial of diabetes progression.	Launched January 2011

Projects Launched/Completed to Date (11) *(continued)*

Project Name/Committee	Execution Objective	Status
Alzheimer's Disease Targeted CSF Proteomics Project (Neuroscience SC)	Qualify a multiplexed panel of known AD CSF-based biomarkers; examine Beta-Site APP Cleaving Enzyme levels in CSF; and qualify a mass spectroscopy panel using Alzheimer's Disease Neuroimaging Initiative CSF samples.	Launched in Q2 2010
Alzheimer's Disease Targeted Plasma Proteomics Project (Neuroscience SC)	Qualify a multiplexed panel of known AD plasma-based biomarkers using plasma samples from the Alzheimer's Disease Neuroimaging Initiative	Launched 12/2008; results anticipated by Q3 2010
PET Radioligand Project (Neuroscience SC)	Develop improved, more sensitive radioligands with higher binding to the peripheral benzodiazepine receptor	Launched 3/2009; two year project
Placebo Data Analysis in Alzheimer's Disease/Mild Cognitive Impairment (Neuroscience SC)	Combine placebo data from large industry clinical trials and analyze them to provide better measures of cognition and disease progression for use in future AD/MCI clinical trials	Launched 12/2009; three year project

Additional Projects Approved/In Development (5)

Project Name/Committee	Execution Objective	Status
Clinical Studies to Evaluate and Qualify Kidney Safety Biomarkers (Executive Committee)	Will compare performance, initiate clinical qualification, and advance regulatory acceptance of new urinary biomarkers of acute drug-induced kidney injury. The Critical Path Institute's Predictive Safety Testing Consortium has successfully qualified for regulatory use in pre-clinical studies a panel of 7 kidney safety biomarkers; this project would expand these findings to the clinical setting.	$3.25M, 2 year project; approved in Q3 2010 (8/2010); working to obtain remaining funding needed to launch project
Endpoints for Clinical Trials of Drugs for Bacterial Infections and Pneumonia (Executive Committee)	Identify and qualify efficacy endpoints for use in regulatory approval of new anti-bacterial drugs on the basis of non-inferiority clinical trials in acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP)	Project concept approved by EC in June 2010; anticipate project plan presentation in Q1/Q2 2011
Osteoarthritis Biomarkers Project (Immunity & Inflammation Steering Committee)	Validate biomarker-based metrics that would serve as putative efficacy end-points in therapeutic development of regimens slowing the progression of knee osteoarthritis by leveraging the unparalleled resources of the NIH Osteoarthritis Initiative	Project plan presented to IISC in January 2011; anticipate request for Executive Committee approval in Q1/Q2 2011
Atherosclerosis Computer Modeling Initiative (Metabolic Disorders SC)	Will aggregate data from existing industry clinical trials to develop a mathematical model of atherosclerosis that integrates and validates known biomarkers.	Approved concept; securing funding commitments and exploring cost/scope reduction
Functional Imaging Biomarkers for Pain and Analgesia (Neuroscience SC)	This project aims to develop imaging as a functional biomarker platform focusing on pain and analgesia. This project also hopes to define standards for the use of fMRI in drug discovery and development trials.	Project plan approved by Executive Committee in February 2010; anticipate ceasing activities around this project due to lack of funding interest