Lessons Learned: Review of Feb 10th IOM Meeting

Friend

IOM

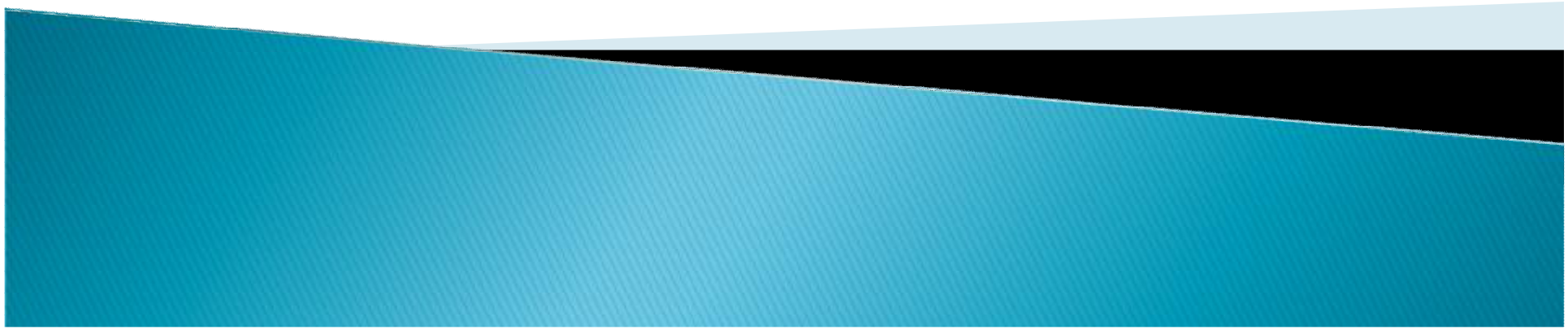
July 22th, 2010

Lessons Learned: Review of Feb 10th IOM Meeting

- Review of Key Examples with Strategies
- Thematic Components of Precompetitive Space

Enabling Precompetitive Collaboration: The I-SPY TRIAL Process

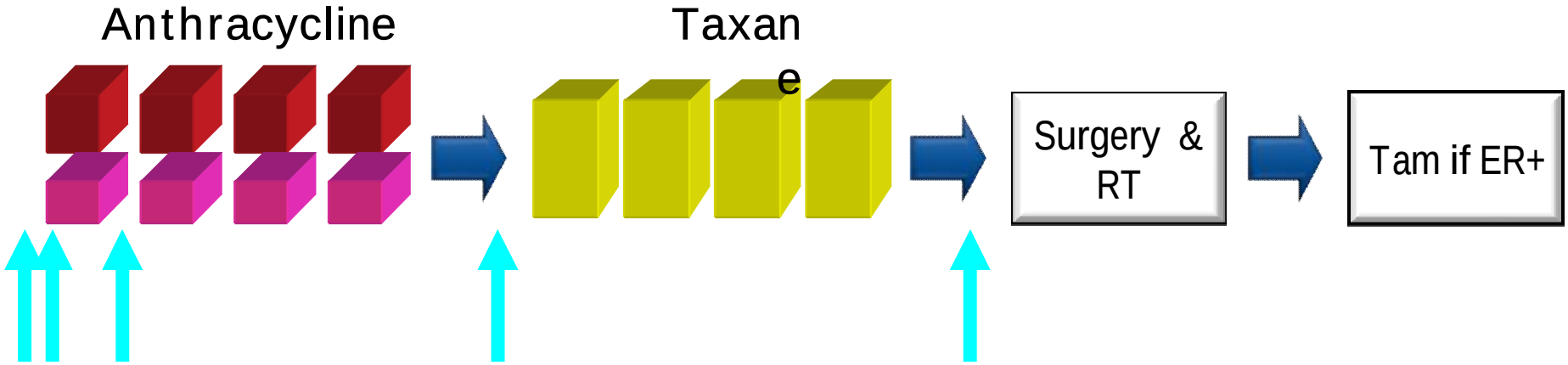
Laura Esserman, MD, MBA
Director, Carol Franc Buck Breast Care Center
Professor of Surgery and Radiology
University of California, San Francisco



I-SPY 1 Clinical Trial Backbone

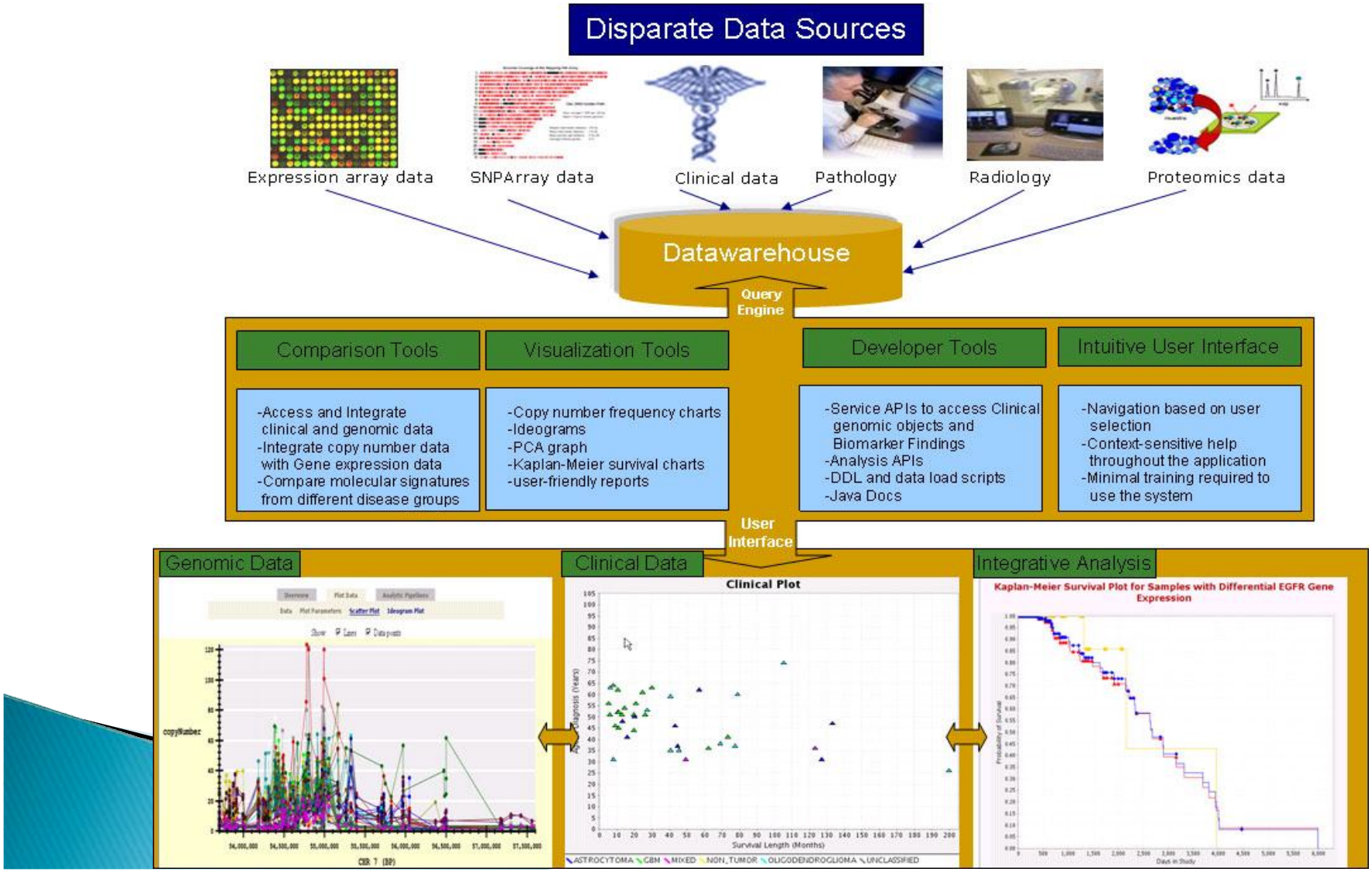
CALGB 150007 / ACRIN 6657

Layered Imaging and Molecular Biomarker Studies Onto Standard Clinical Care



- Serial MRI Scans
- Serial Core Biopsies

caINTEGRATOR 1 Built To Instantiate Data Sharing



Value Proposition/Benefit for Partners in Public Private Partnership (PPP)

Patients	§ Opportunity to Drive Path to Personalized Treatment § Potentially More Effective Treatment/Management
FDA	§ Provides for Evidence-Based Regulatory Policy
Pharma	§ More Efficient Drug Development and Approval Path § Better Early Response Criteria
Device Industry	§ Larger Markets § Less Risk
CMS	§ Helps Define Reasonableness and Need
Academia/NCD	§ Better Clinical Data § More Effective Treatment/Management

The AZ-Merck Collaboration

Institute of Medicine
Washington, D.C.
10 Feb 2010

Pearl S. Huang, Ph.D.
VP Oncology, Merck and Co.
On behalf of the AZ/Merck Collaboration Team

Collaboration Announced

THE WALL STREET JOURNAL.

MONDAY, JUNE 1, 2009

AstraZeneca, Merck to Test Cancer Drugs in 'Cocktail'

By Ron Winslow

ORLANDO, Fla. -- Merck & Co. and AstraZeneca PLC plan to announce Monday an unusual agreement to test a potential new cancer regimen composed of two experimental agents that are still in early human trials and several years away from reaching the market.

The collaboration, sparked by an encounter between scientists from the companies in an airport security line in Dublin, is based on laboratory evidence that the two compounds given in combination could have a much more potent effect against tumors than each may have as separate treatments. Merck and AstraZeneca scientists say the treatment could prove effective against several types of cancer.

The drugs -- MK-2206 from Merck and AZD6244 from AstraZeneca -- are candidates for the burgeoning arsenal of so-called targeted treatments that is transforming cancer care by disrupting whether combining the drugs will improve survival over Nexavar alone in patients with advanced liver cancer.

Merck, Whitehouse Station, N.J., and AstraZeneca are announcing the collaboration during the annual scientific meeting of the American Society of Clinical Oncology in Orlando. They say they are the first large pharmaceutical companies to join forces to test a combination treatment with compounds so early in development. AZD6244, which blocks a pathway known as MEK, has been tested in early-to-midstage trials in patients with skin, colorectal and lung cancers. Merck's drug, which inhibits a pathway called Akt, has been shown to have activity against tumors in a handful of patients in an early-stage test.

MEK and Akt "are two critical pathways in oncogene signaling," said Gary Gilliland, senior vice president and franchise head for oncology at Merck Research Laboratories. "If we shut down compounds together, he seemed "bewildered," she recalls. It wasn't public knowledge that Merck was developing an Akt inhibitor. But by the end of the conversation, they both agreed to take the idea to their respective companies. "We immediately clicked," she says. In an email message, Dr. Smith said he recalls thinking that being hailed as "the MEK guy" was an unusual greeting in a public place.

Even though AstraZeneca was working on its own Akt blocker and Merck was developing an MEK inhibitor, the companies say they determined that joining forces would offer a chance to get a treatment to market quicker.

The companies initially crafted an agreement to do lab studies to see if the science supported moving ahead with human tests of the combination. They cleared that hurdle. The new pact calls for the companies to share costs of testing the compounds in an early-stage

Features of the Collaboration Agreement

- Staged agreement: preclinical and clinical.
- Joint governance, decision rights and shared costs.
- Freedom of operation for both parties: multiple combination studies with similar agents can occur independently and in parallel.
- Intellectual Property shared by inventors.

ENGELBERG CENTER for Health Care Reform at BROOKINGS

Achieving the Promise of Personalized Cancer Therapy: The role of public-private collaboration

Mark McClellan, MD, PhD
Director, Engelberg Center for Health Care Reform
Leonard D. Schaeffer Chair in Health Policy Studies
The Brookings Institution

February 10, 2010

Some key elements of a successful collaboration

- Neutral convener
  - Needs to bring all relevant stakeholder perspectives
  - Legal safe harbor for collaboration
  - For cancer: FDA and global regulators, NCI, developers, manufacturers, clinical researchers, basic science community, patient and consumer advocates
- Effective management
  - Efficient operation requires experienced, full-time management
  - Governance structure that allows collaborators to drive strategy
  - Promote economic and intellectual sustainability
- Sufficient incentives
  - Must overcome existing incentives to compete with new incentives to collaborate in academia and private sector
  - Develop policies that reward development of shared data repositories and infrastructure for effective collaboration

Considerations for Incentives

- Support for process: direct payments for infrastructure, payments for participation or reporting
- Support for results: payments for achievement of (well-defined) outcomes
- Infrastructure for data exchange and meaningful analysis vs. use of the network for results

More efficient development and availability of effective targeted cancer therapies requires…

- Identification and prioritization of "bottleneck" knowledge gaps, and which can likely be addressed more effectively through precompetitive collaboration
- Incentives to develop information "utilities":
  - Data standards
  - Data infrastructure
- More head-to-head evaluations of collaboration models to identify key features and best practices
- Full participation of the cancer community in research collaborations, *especially FDA and patients*
- Less regulatory uncertainty—a "critical path" for drug-diagnostic pairs in cancer
- Effective incentives for collaborative research, especially on disease models and biomarker qualification

CRITICAL PATH INSTITUTE

Why Medical Product Development Has Special Requirements

Raymond L. Woosley, MD, PhD

President and CEO

Critical Path Institute

Coalition Against Major Diseases

CRITICAL PATH INSTITUTE

Engelberg Center

CAMD

Patients Government Industry

NIH

Summary: Needed for Innovative Drug Development

CRITICAL PATH INSTITUTE

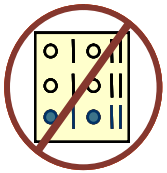
- Common data elements in development
- Biomarkers "qualified for use"
- Independent certification that the biomarker assays perform as intended (Analytic Validity in the Field)
- Innovative tools/methods for trial design
  - Adaptive clinical trial design
  - Trial simulation using disease models
- Innovative Business Models

The Case for Enabling Distributed Innovation

Karim R. Lakhani (Harvard Business School)

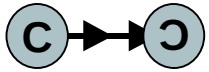
Open Source Principles

Intellectual property



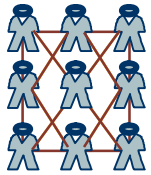
Code should always be open - "Free speech, not free beer"

"Copyleft"



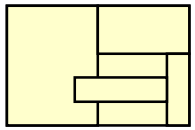
"Use copyright to ensure copyleft"

Development paradigm



Extensive involvement of user/developer community

"Release early, release often"

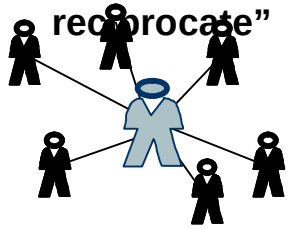


Modularize code

Resource model

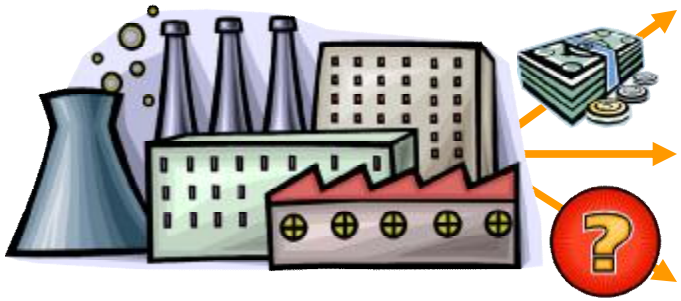
Good ideas come from solving a problem or scratching an itch

"The three obligations: to give, to receive, to reciprocate"

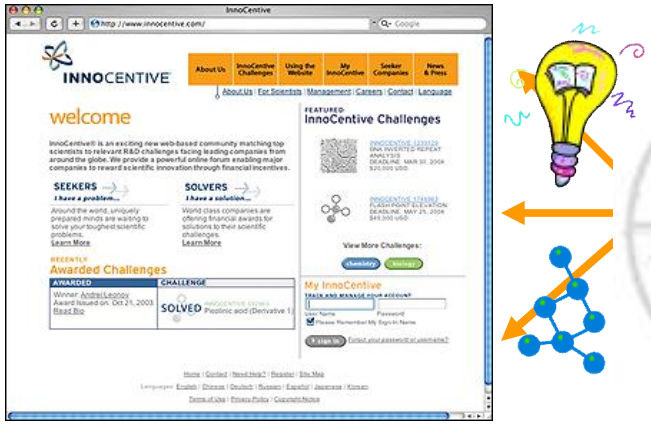


Peer leadership - vision, engagement, code

InnoCentive as a Modern Implementation of Innovation Contests



R&D Labs



Knowledge Broker

110,000 independent scientists

Context:

1. **R&D Labs inside of major multinationals are not able to solve certain scientific problems**
   - **Their own internal and external experts cannot obtain solutions**
2. **Hope to get solution by going to distributed scientists that they do not know who may have an answer**

Myelin Repair Foundation Created Infrastructure for Collaborative Science Research

History

- Scott Johnson – Founder Diagnosed with MS 30 Years
- Frustrated with lack of progress in MS research
- Realized most problems are multi-causal and multi-disciplinary but R&D is organized sequentially (at best) results in a Science Gap and Commercial Gap
- In 2005, organize a team based research consortium of 5 labs in 5 institutions to *find treatment* for MS
- Labs represent expertise in: neurobiology, genetics, cellular models, animal models, proteomics and immunology
- Collectively generate 100 questions that need to be answered to develop joint research program

Results in three years

- 18 novel targets identified – 8 moving forward for further development
- >25 papers in peer reviewed journals
- 10 new tools for accelerating research (Databases, animal models, testing platforms)
- 7 patents

Key Issues for Pharmaceutical Pre-Competitive Collaboration

- IP sharing
  - Culture change for most firms used to secrecy
  - Appropriate vehicles (e.g.: non-profits) for holding IP
  - Academic partner IP issues (publications)
- Coordination role
  - How will the work be coordinated?
- Determining joint objectives for participation
- Resource sharing agreements
  - People
  - Materials
  - Approaches
- Conditions for entry, exit and ending

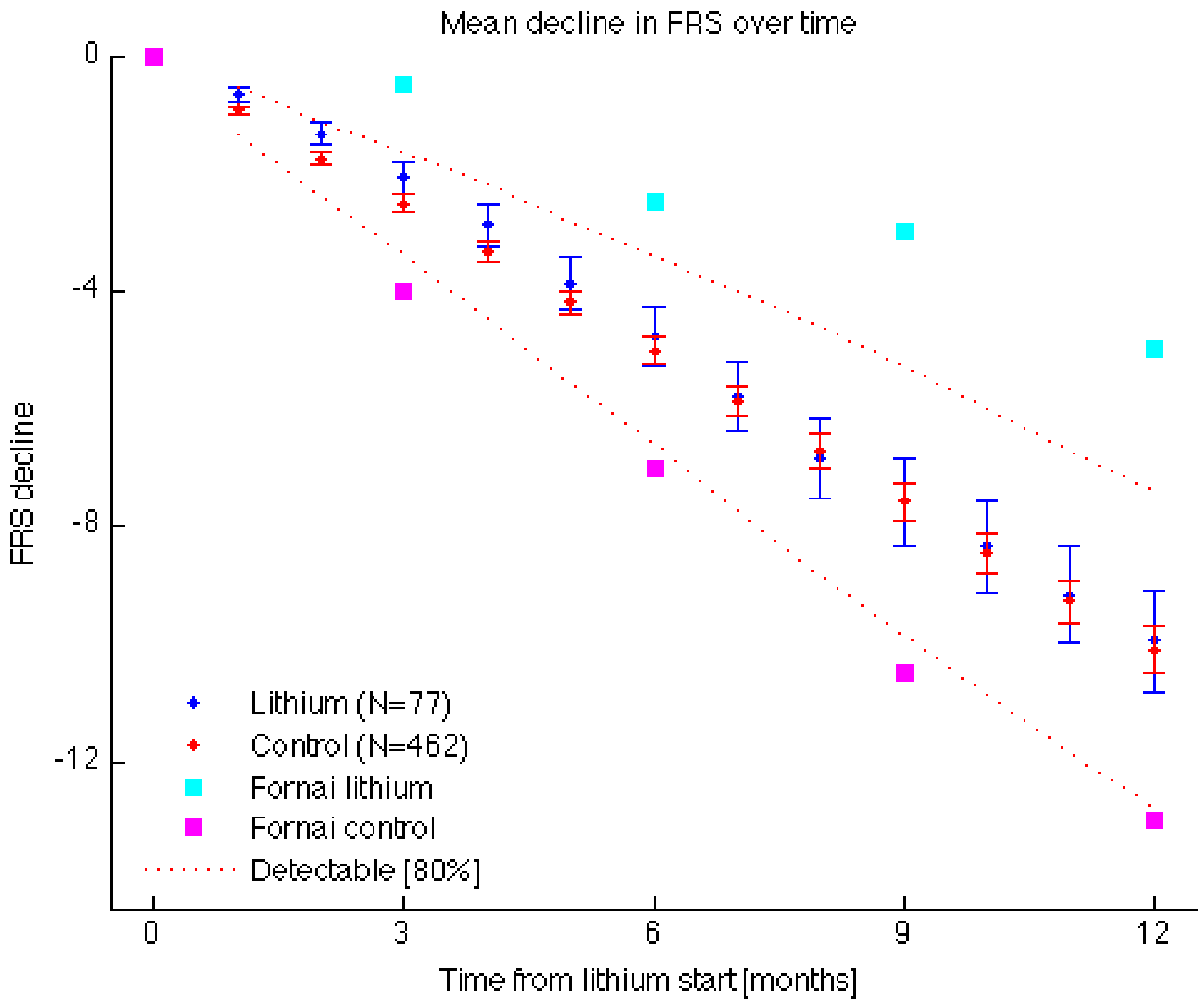
James Allen Heywood

Institute of Medicine

"All models are wrong, but some are useful."

George Edward Pelham Box


Stopped Using
Deceased
Patient
Profile Star
Onset Date
Diagnosis Date
Type
Sex
Age
Current Star
History Star
# of FRS scores
Onset to Start
Start to Today
# of data points in months before and after Lithium start
-1 0 1 2 3 4 5 6
humberto-from-brazil
4
12
0
1 1 1 1 1 1 1
ALS: 2 yrs
humberto-from-brazil
Male, 43 years
Onset: Arms
On Rilutek
Blood Level
0.2 mmol/L
Lithicarb
150 mg/day
FRS
17
FVC
40
Started Lithium
mmol/L
0.8
0.4
mg/day
900
600
300
48
40
32
24
16
8
Side Effects
Constipation Slurred speech Excessive saliva Weight gain or loss Depression Muscle weakness, stiffness, twitching, or tightness Joint or muscle pain Tiredness


Mean decline in FRS over time
0
-4
-8
-12
FRS decline
0
3
6
9
12
Time from lithium start [months]
Lithium (N=77)
Control (N=462)
Fornai lithium
Fornai control
Detectable [80%]

National Cancer Institute

National Human Genome Research Institute

The Cancer Genome Atlas

IOM Workshop

February 9-10, 2010

Joe Vockley, Ph.D.

Director, TCGA Program Office

Bethesda, MD

Precompetitive Collaboration in Oncology: Imaging Science

Institute of Medicine

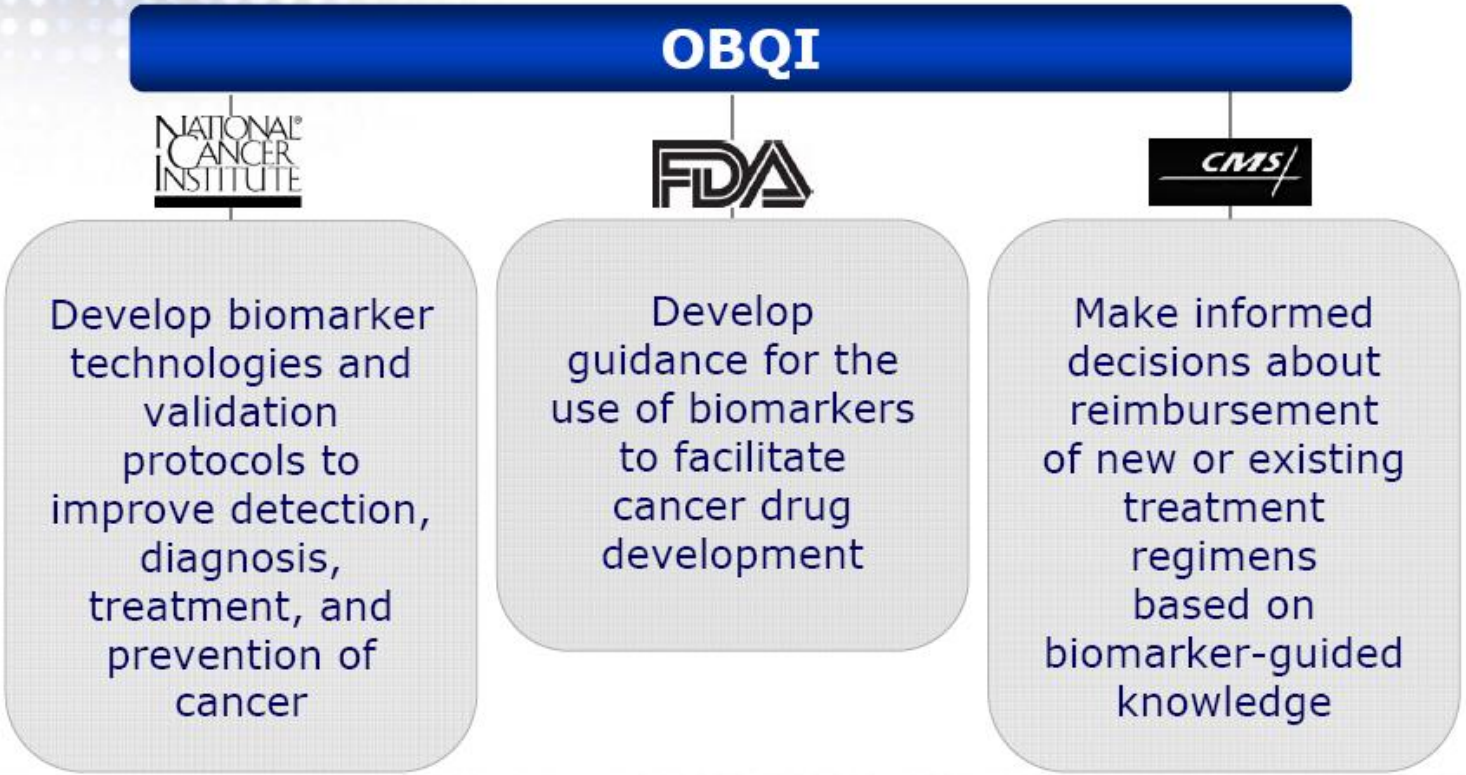
February 10, 2010

Gary J. Kelloff, MD
National Cancer Institute

Value Proposition/Benefit for Partners in Public Private Partnership (PPP)

- Patients: Better Clinical Data, More Effective Treatment/Management
- FDA: Provides for Evidence-Based Regulatory Policy
- Pharma: More Efficient Drug Development and Approval Path, Better Early Response Criteria
- Device Industry: Larger Market for PET/CT and PET/MRI Scanners
- CMS: Helps Define Reasonableness and Need
- Academia/NCI: Better Clinical Data, More Effective Treatment/Management

OBQI Coordinates Cross-HHS Goals for Biomarker Validation and Clinical Use



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Cooperation in Semiconductor R&D; Lessons from SEMATECH

WJ Spencer,
Chairman Emeritus
SEMATECH

Accelerating the next technology revolution.

Open Innovation Networks:
An Imperative for Breakthrough Therapies

Neal H. Cohen, MD, MPH, MS
Vice Dean
Professor, Anesthesia and Medicine
UCSF School of Medicine

August 8, 2008

What drives current behavior?

Extending the Spectrum of Pre-Competitive
Oncology Biomedical Research

Sharing Consultants

Trading Scientists

Sharing Revenues

Sharing Analysis Tools

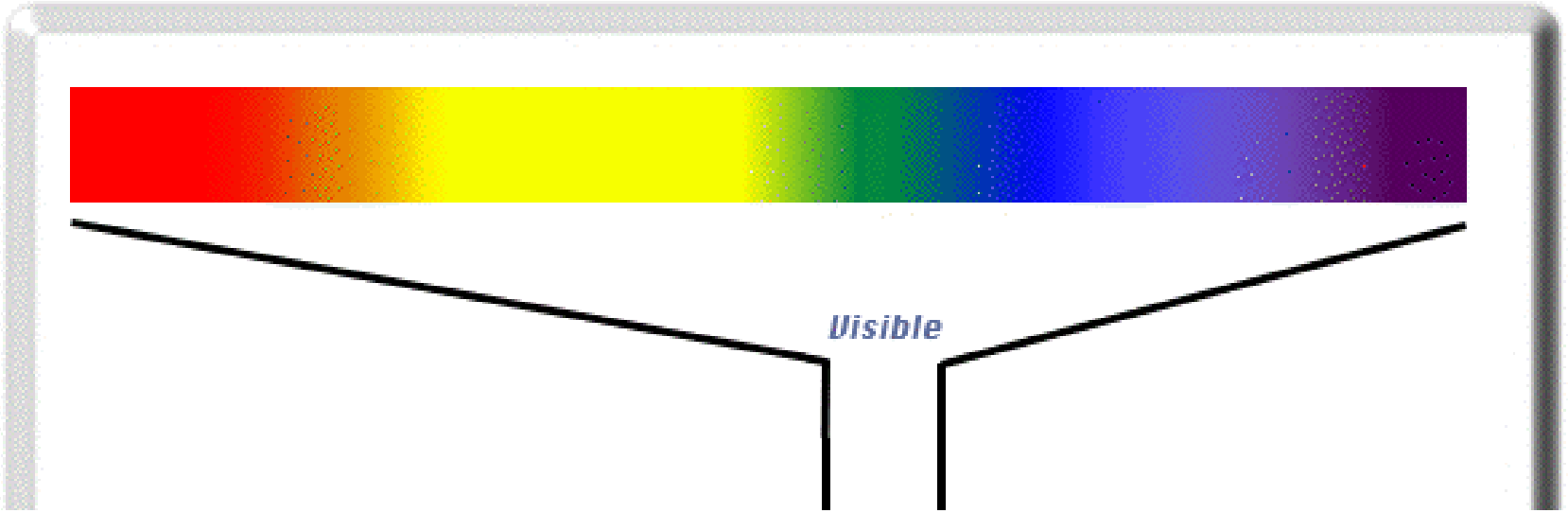
Sharing Samples and
Non-Compound Data

Sharing Disease Models

Sharing Clinical Compound Data

Sharing Toxicities

Sharing Compounds



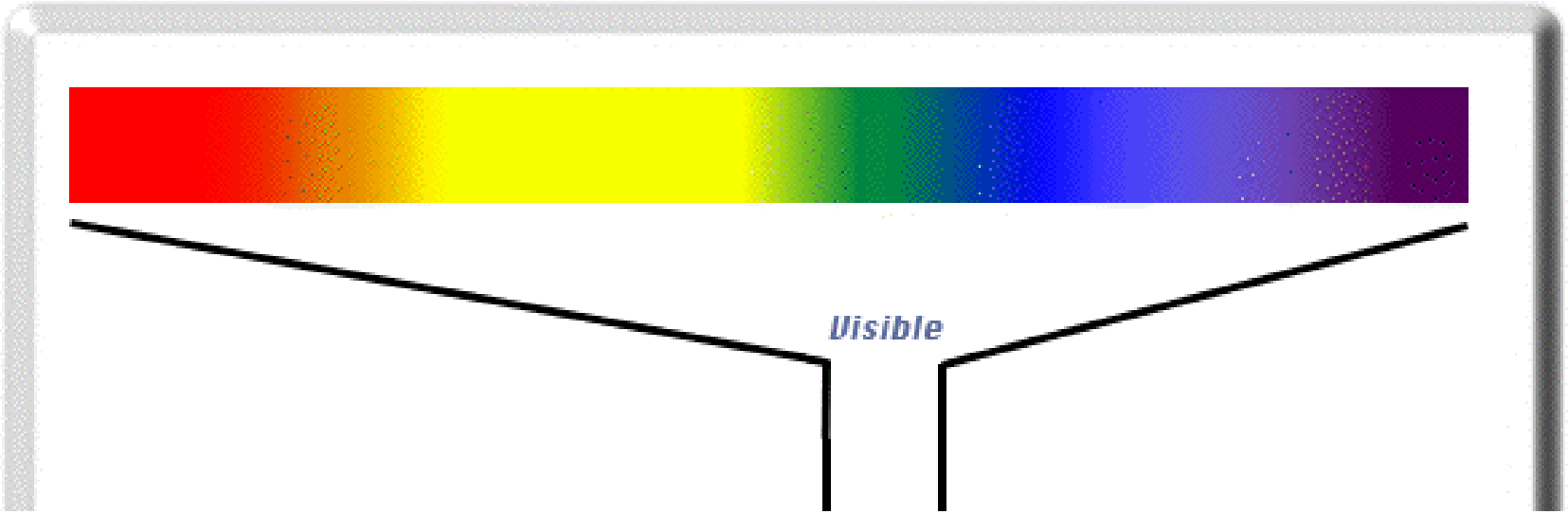
Extending the Spectrum of Pre-Competitive
Oncology Biomedical Research

Remember that if it is a company and often also if a University
they are obligated to justify
the underlying business case

Sharing ← Disease Models → Unsharing

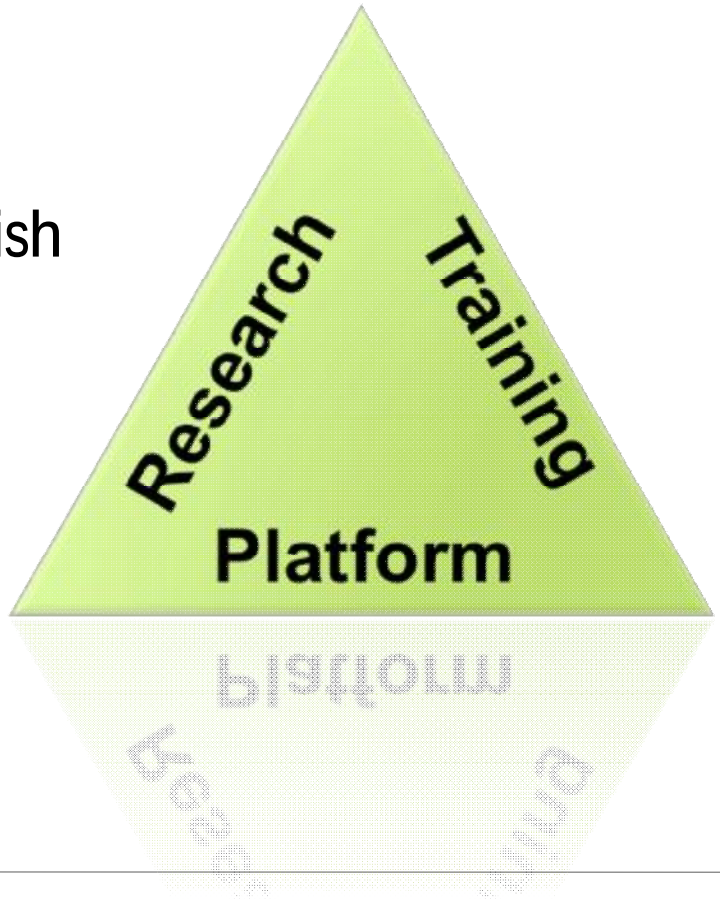
Benefits **Costs**

Can I get there without others cheaply?
Will others beat me to it if I do not join?
Can I build a first mover advantage?
Can I sustain my advantage and sustain my return?



Sage Bionetworks Strategic Priorities

- Integrative genomics and network biology research
- Repository and tools to establish the Commons platform
- Interdisciplinary scientist training to enable widespread participation



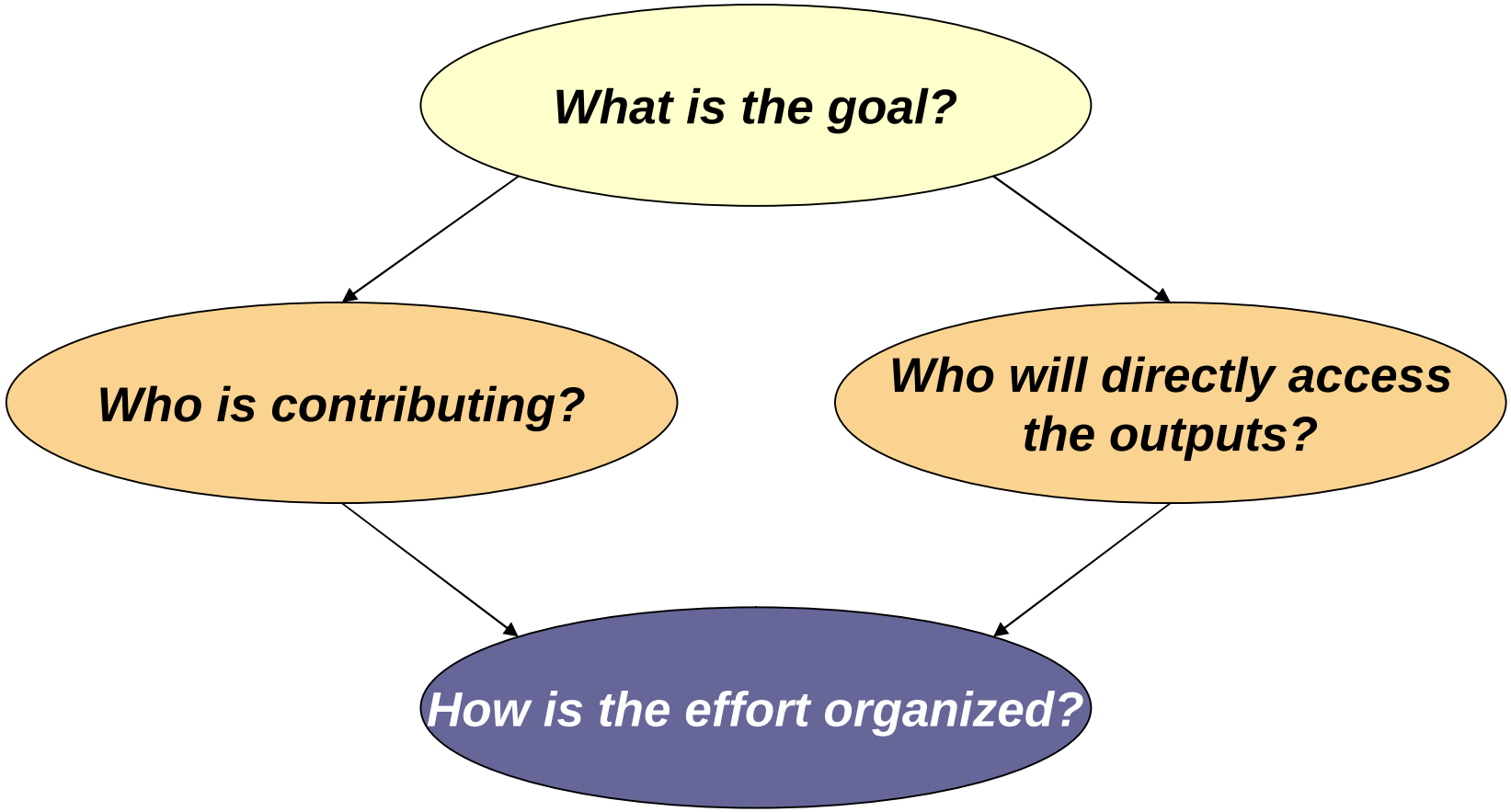
Sage BIONETWORKS

Overview of Precompetitive Collaboration for Institute of Medicine Workshop

February 10, 2010

altshulergray

Framing the phenomenon



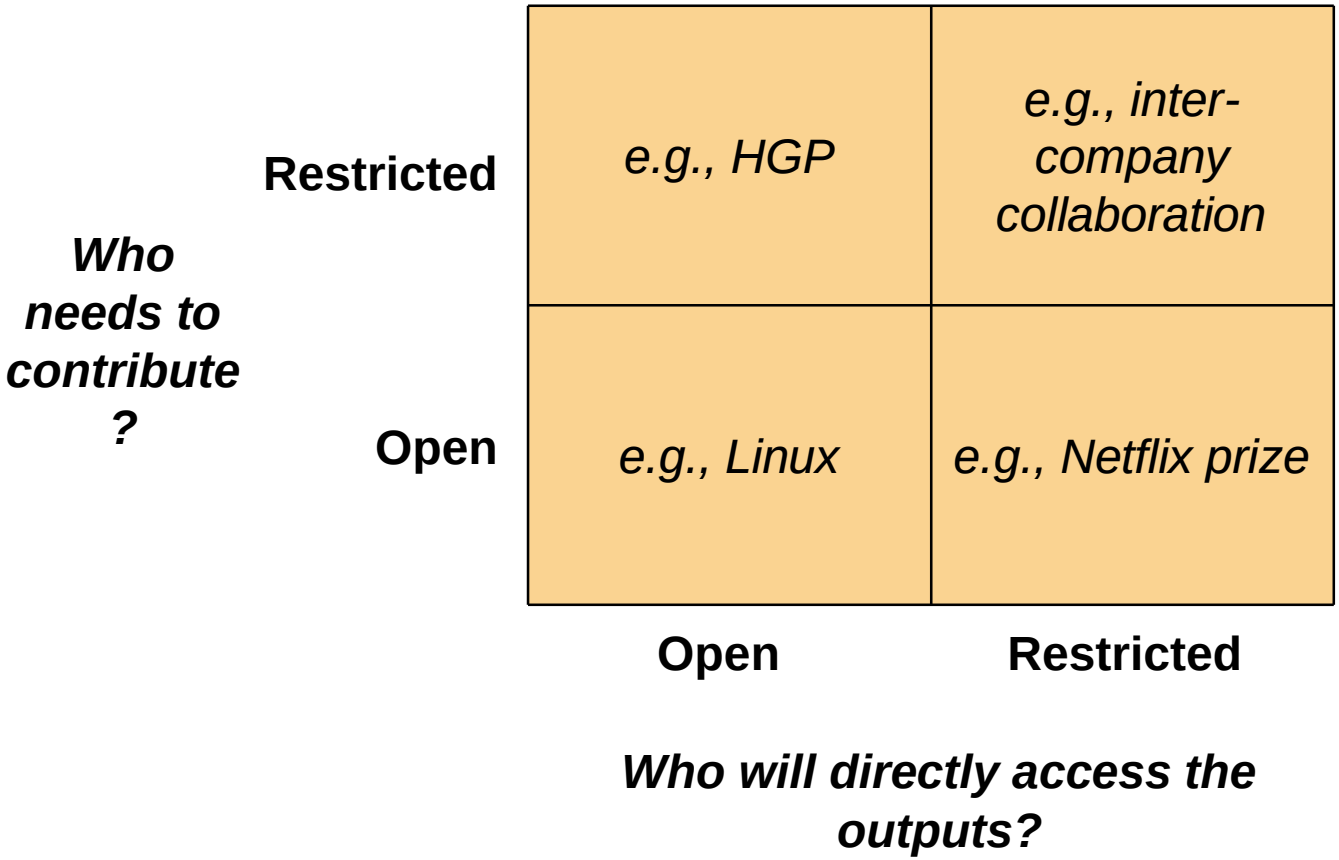
Who are the players?

How open/closed is the collaboration?

	Who needs to contribute?	Who will access the outputs?
Collaboration more likely to be open if…	• Low barriers to entry • Need for quantity of input outweighs quality control • Novel perspectives are sought from diverse fields	• Output cannot be directly monetized • Problem would benefit from ongoing development
Collaboration more likely to be restricted if…	• High barriers to entry (e.g., cost of equipment) • Need for high levels of coordination and quality control	• Output closer to commercialization • Tied to cost to fund the effort – to avoid free riders • Proprietary IP in outputs

Who are the players?

Open vs. closed: four possible combinations



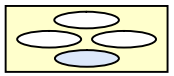
Inter-organizational research collaborations

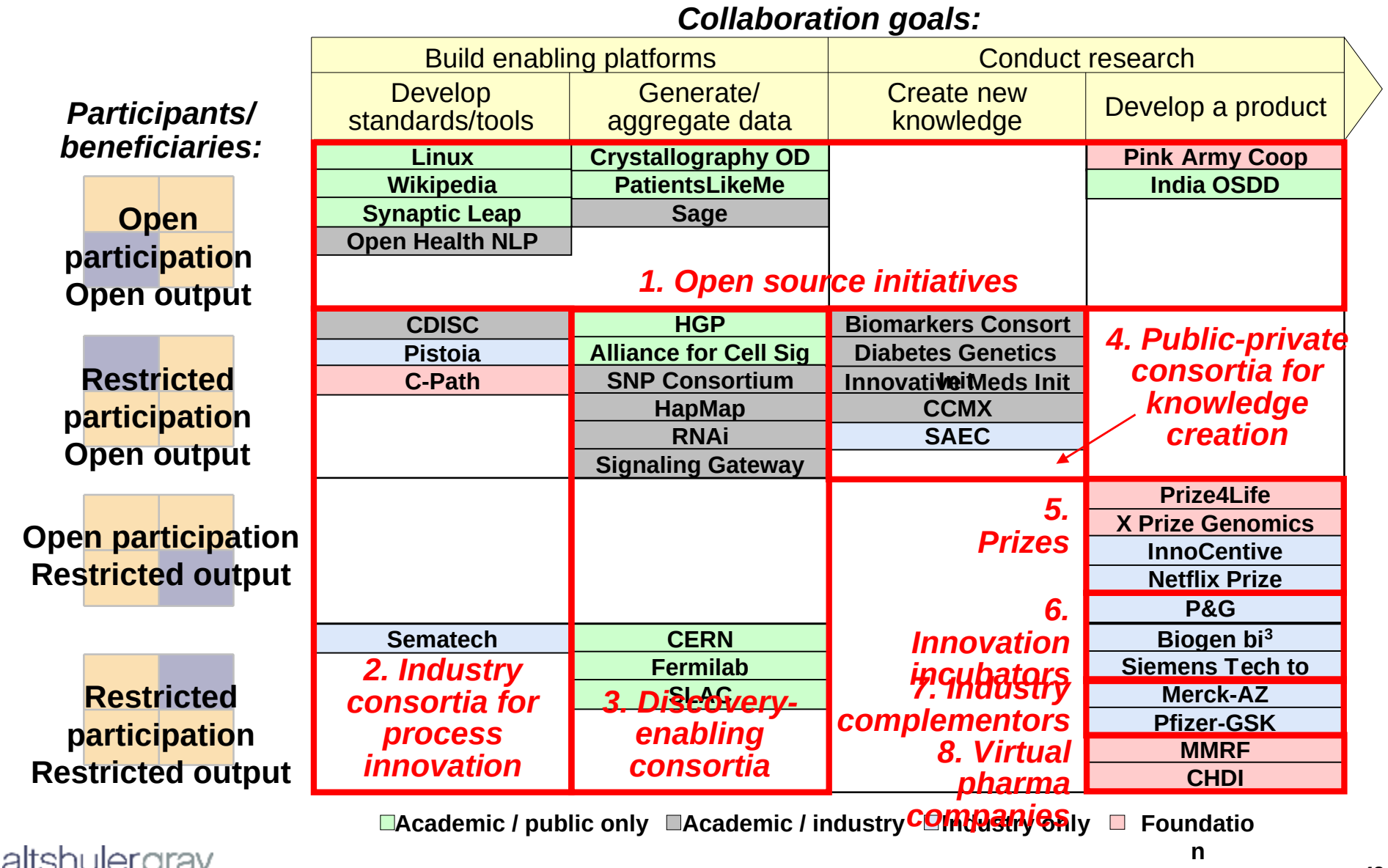
Collaboration goals:

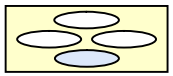
Participants/ beneficiaries:	Build enabling platforms		Conduct research	
	Develop standards/tools	Generate/ aggregate data	Create new knowledge	Develop a product
Open participation Open output	Linux Wikipedia Synaptic Leap Open Health NLP	Crystallography OD PatientsLikeMe Sage		Pink Army Coop India OSDD
Restricted participation Open output	CDISC Pistoia C-Path	HGP Alliance for Cell Sig SNP Consortium HapMap RNAi Signaling Gateway	Biomarkers Consort Diabetes Genetics Innovative MedsInit CCMX SAEC	
Open participation Restricted output				Prize4Life X Prize Genomics InnoCentive Netflix Prize P&G
Restricted participation Restricted output	Sematech	CERN Fermilab SLAC		Biogen bi^3 Siemens Tech to Merck-AZ Pfizer-GSK MMRF CHDI

Academic / public only Academic / industry Industry only Foundation

Eight models of precompetitive collaboration







Eight models of precompetitive collaboration

1. Open source initiatives
2. Industry consortia for R&D process innovation
3. Discovery-enabling consortia
4. Public-private consortia for knowledge creation
5. Prizes
6. Innovation incubators/insourcing
7. Industry complementor relationships
8. Virtual pharma companies

Lessons Learned: Review of Feb 10th IOM Meeting

- Review of Key Examples with Strategies
  - Multiple proof of efforts within and outside drug discovery
- Thematic Components of Precompetitive Space
  - Diverse approaches for diverse goals
  - Cultural vs technical barriers
  - Requires neutral well funded coordination with incentives to all