Disruptive Innovation at the National Institutes of Health

Kathy Hudson, Ph.D.
Deputy Director for Science, Outreach, and Policy, NIH

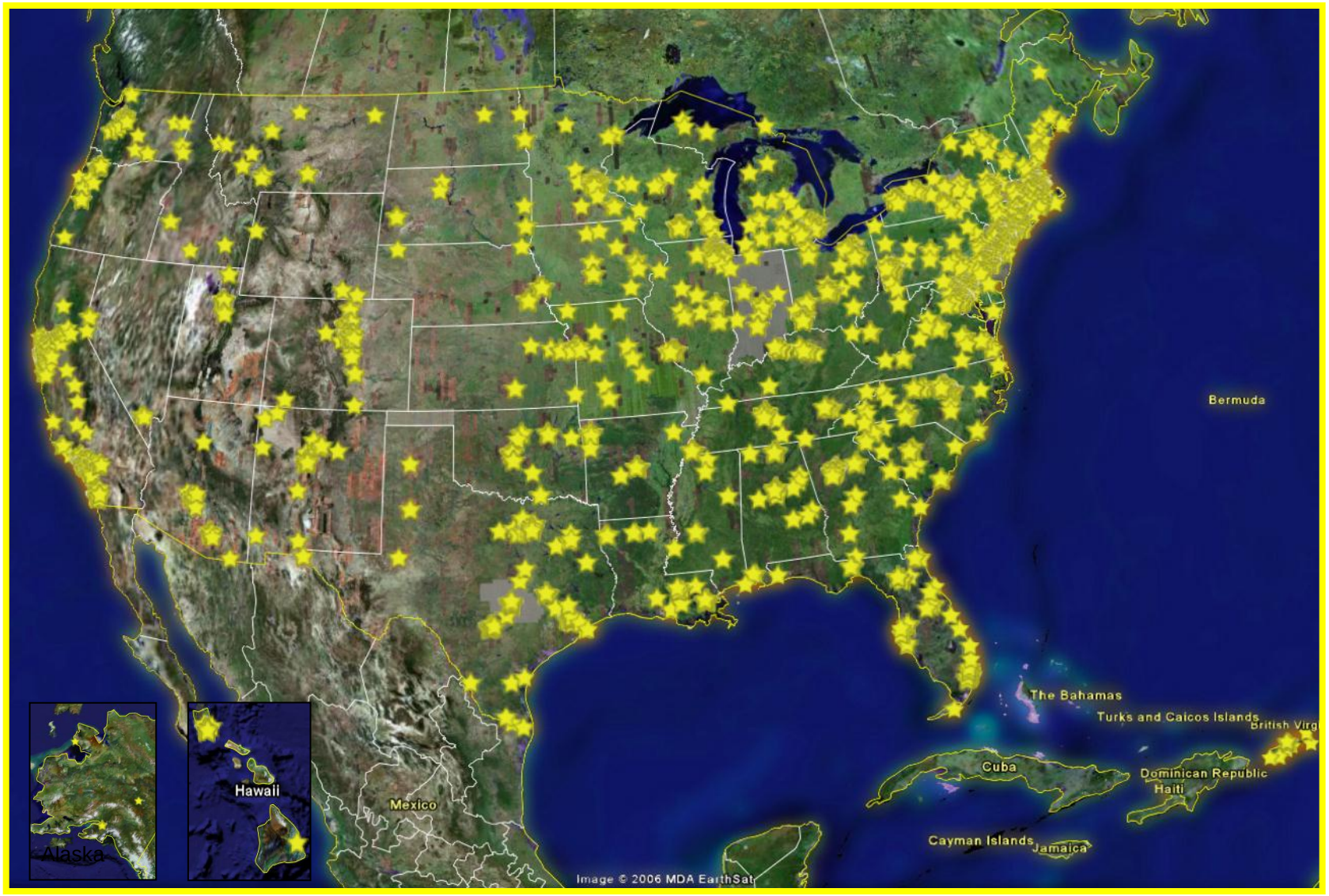
December 1, 2011

NIH Mission

… to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability.

President Franklin D. Roosevelt at NIH dedication; October 31, 1940

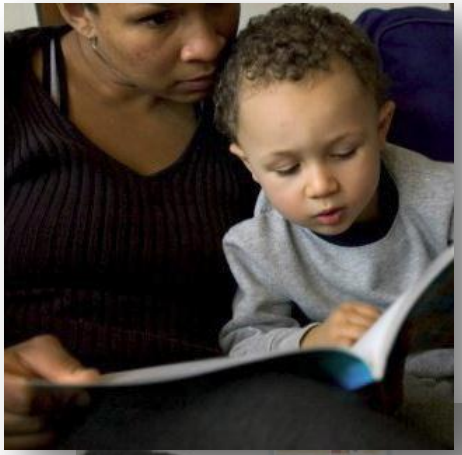
NIH Funds Scientists Across U.S.

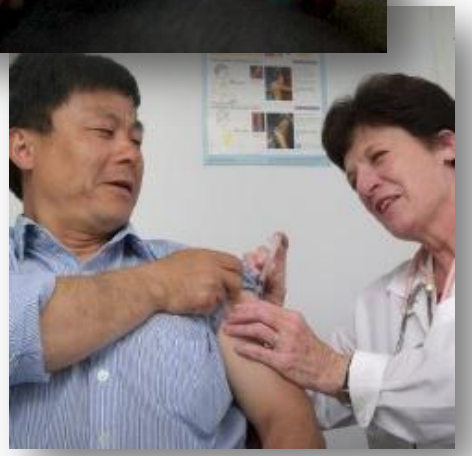


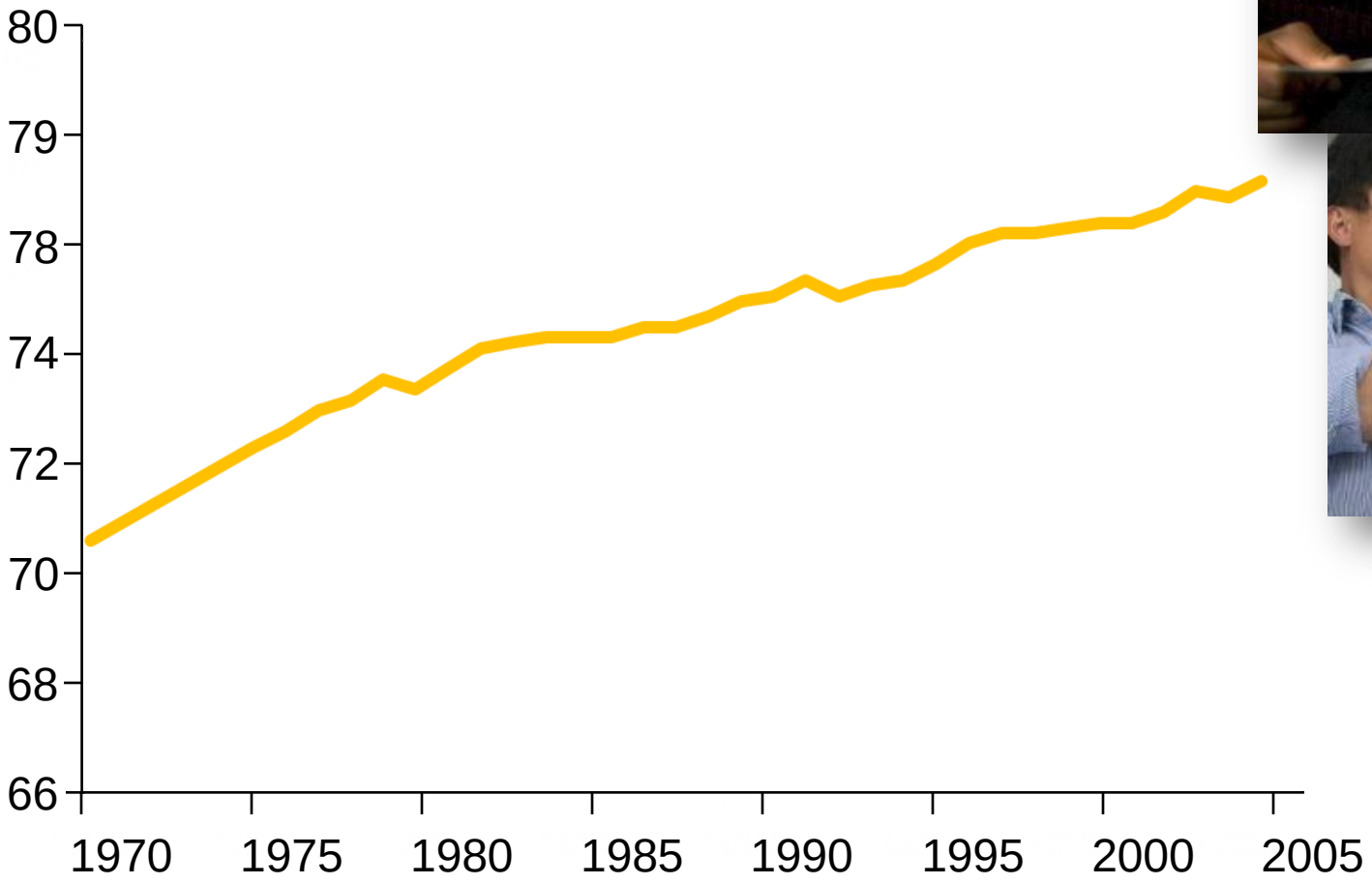
Data: Assoc of University Technology Managers (AUTM) Survey 2004

. . .and around the globe . . .

The Benefits of Biomedical and Public Health Advances U.S. Life Expectancy



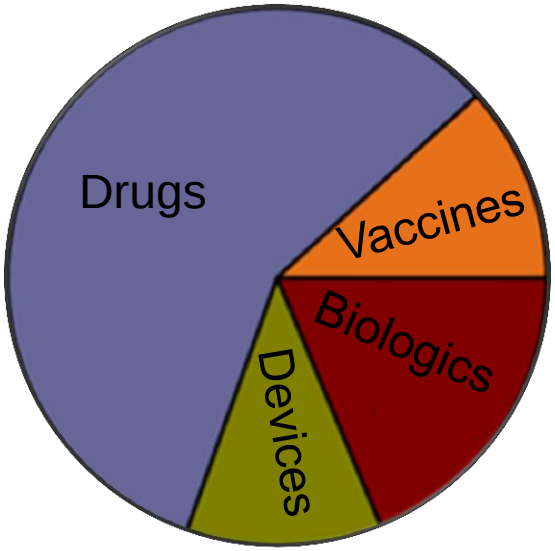




Source: CDC National Vital Statistics Reports, Vol 57, No 14, April 17, 2009

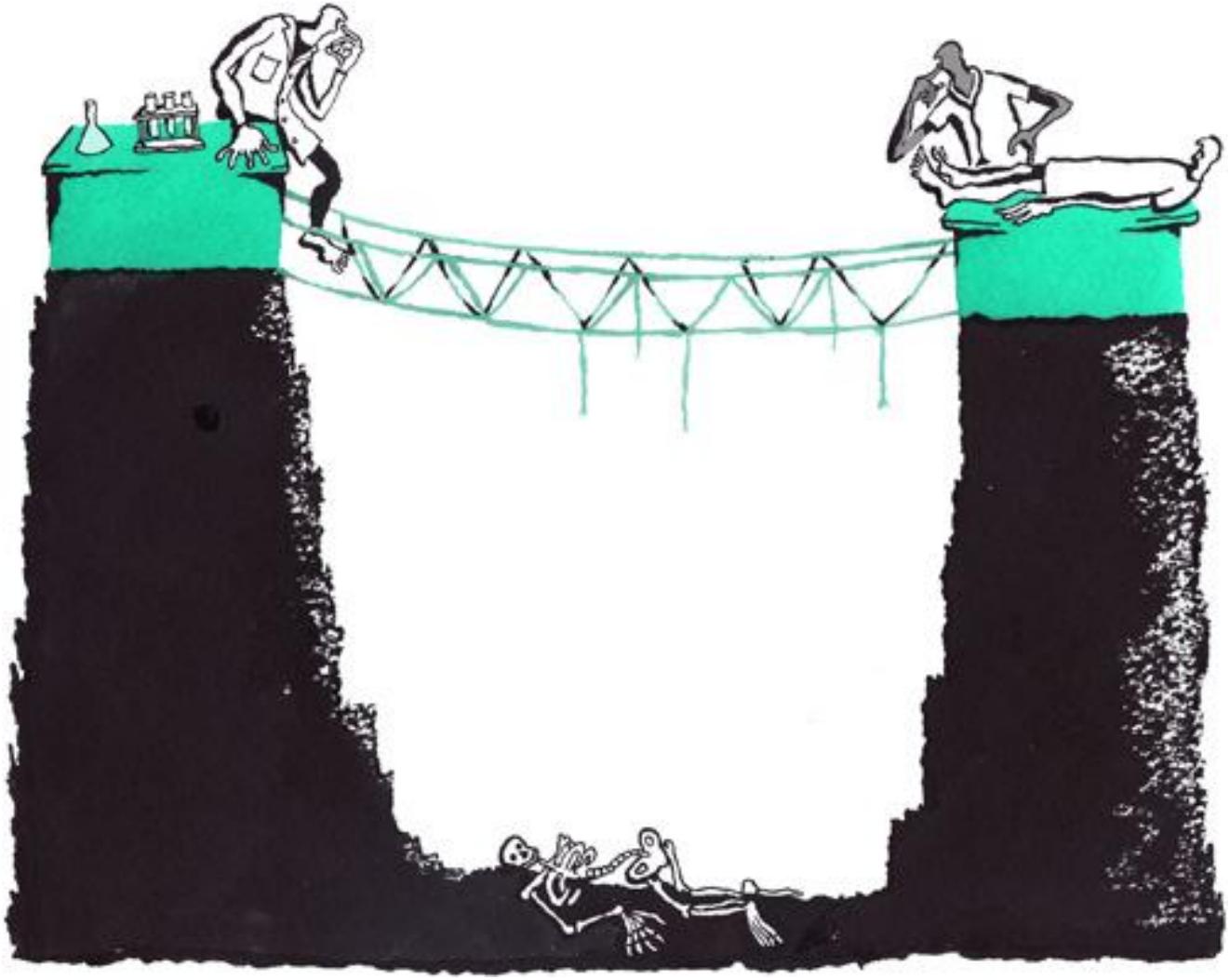
Therapeutics Development at NIH

- A 2010 trans-NIH inventory of activities relevant to therapeutics development found:
- Substantial investments in therapeutics development research
- Approximately 65% for preclinical research; 35% clinical research
- 550 activities reported of varying sizes and areas of emphasis

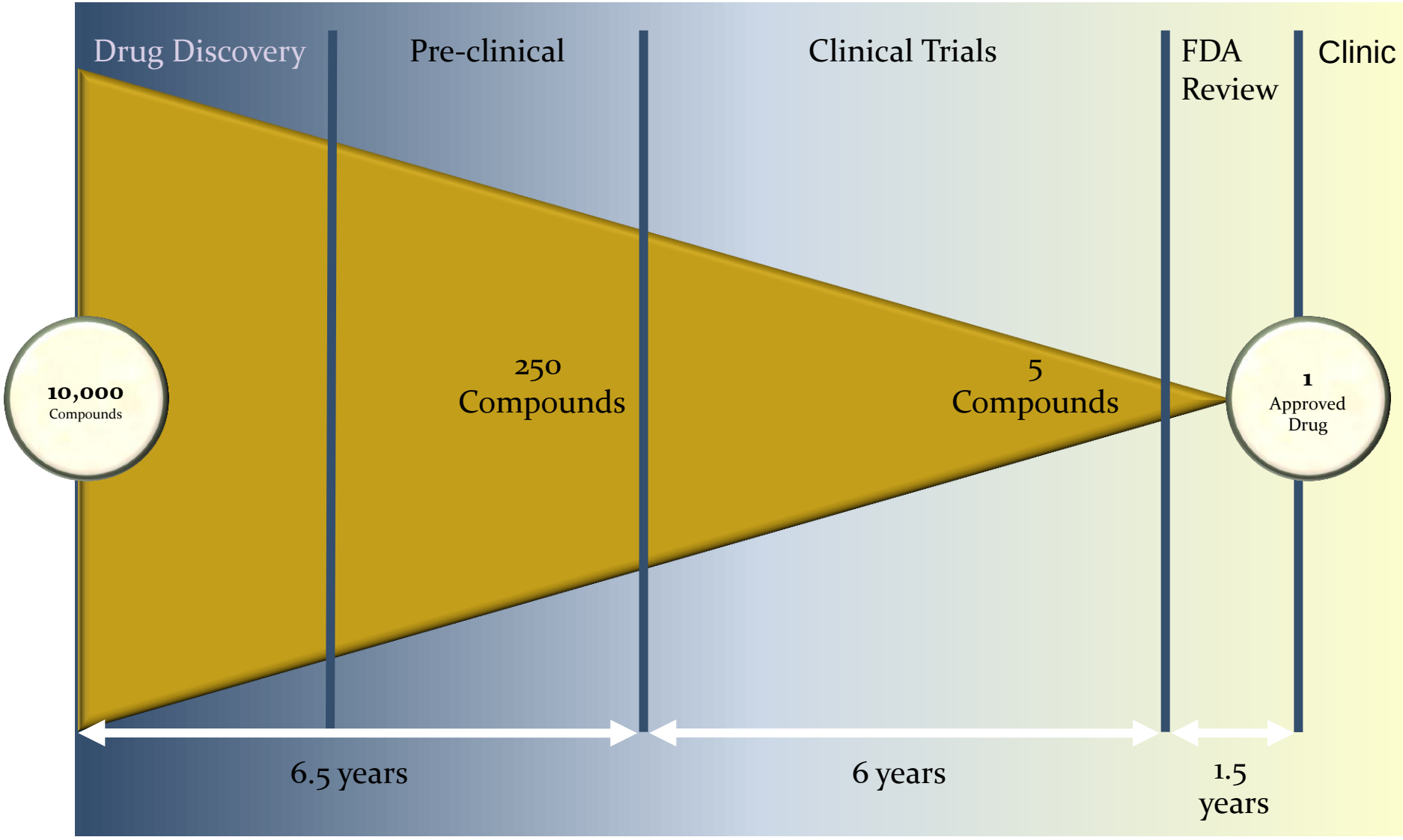


Distribution of Investment

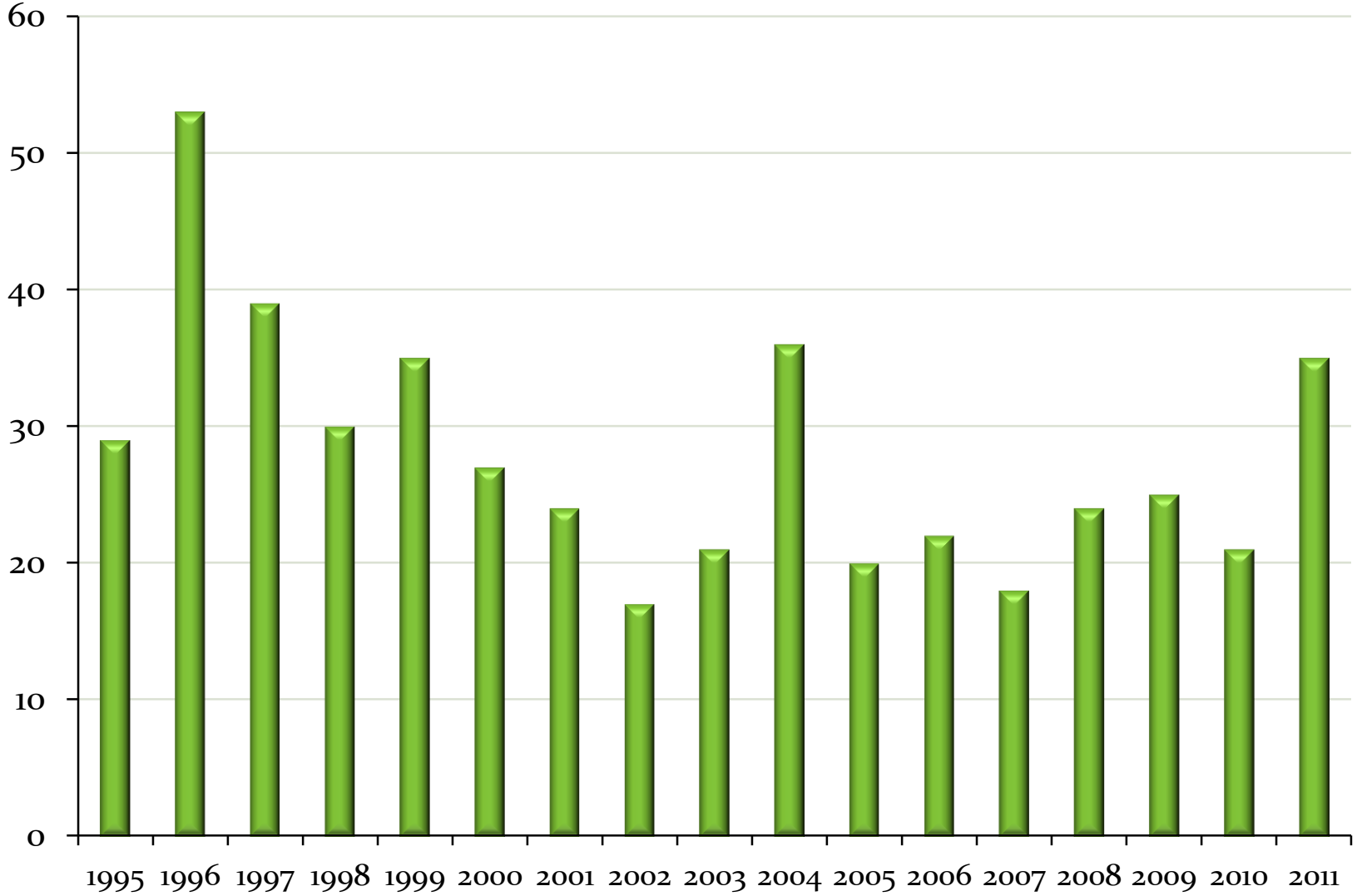
Valley of Death



The Problem: Development of New Therapeutics is Slow, Expensive, and Failure-Prone



New Medicines in Your Medicine Cabinet: New Molecular Entities Entering Marketplace



Source: FDA

Pursuing Opportunities for Disruptive Translational Innovation

POLICY www.ScienceTranslationalMedicine.org 6 July 2011 Vol 3 Issue 90 90

Reengineering Translational Science: The Time Is Right

Francis S. Collins

Despite dramatic advances in the molecular pathogenesis of disease, translation of basic biomedical research into safe and effective clinical applications remains a slow, expensive, and failure-prone endeavor. To pursue opportunities for disruptive translational innovation, the U.S. National Institutes of Health (NIH) intends to establish a new entity, the National Center for Advancing Translational Sciences (NCATS). The mission of NCATS is to catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of diseases and conditions. The new center's activities will complement, and not compete with, translational research being carried out at NIH and elsewhere in the public and private sectors.

"My administration is announcing a new center that will help companies reduce the time and cost of developing lifesaving drugs."

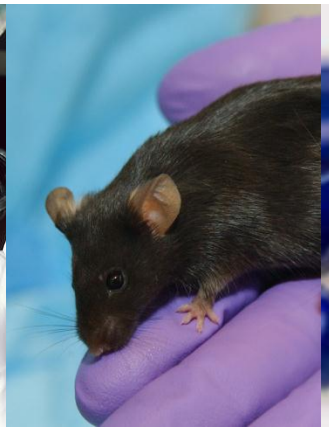
President Obama
Signing of America Invents Act
Thomas Jefferson High School
September 16, 2011

NCATS:
Pursuing Opportunities for Disruptive Innovation

Mission:

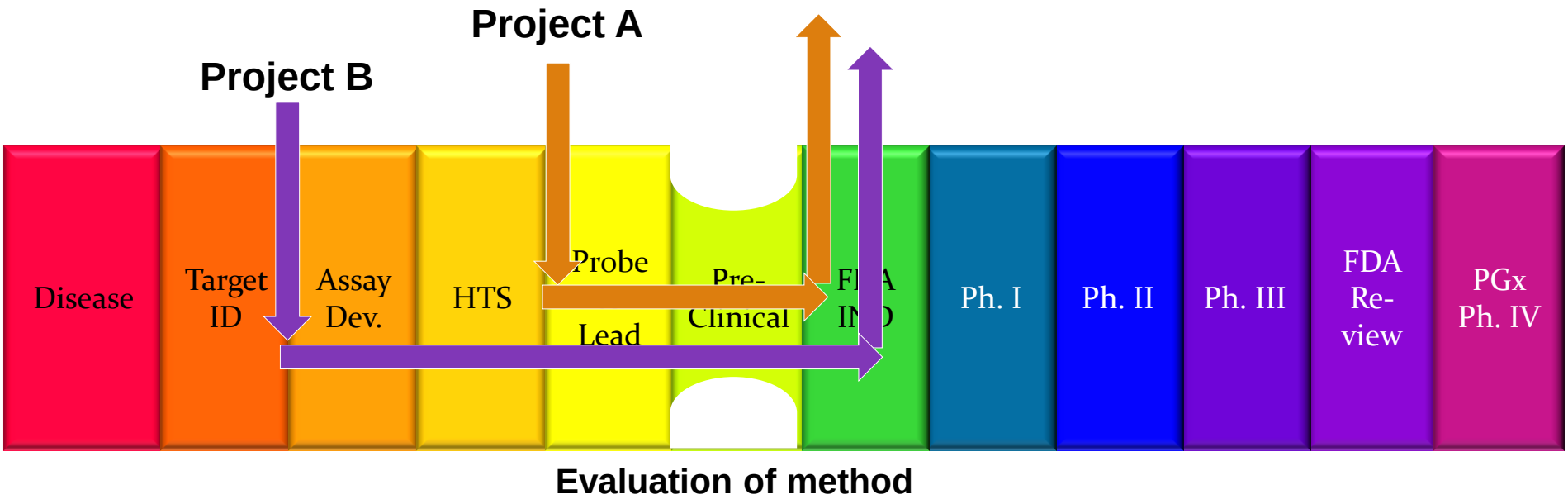
To catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions





Advancing the Science of Translation

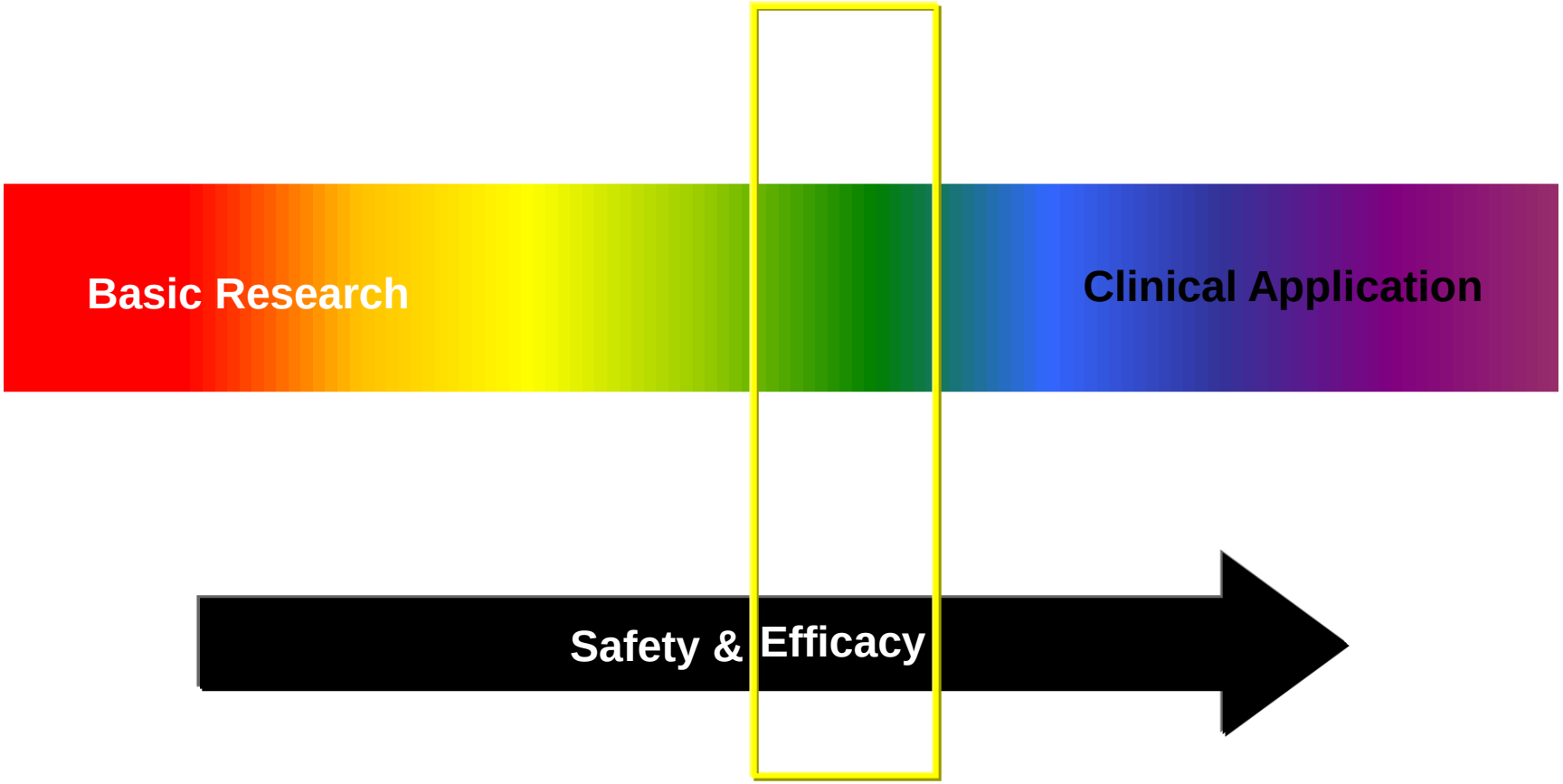
- Study the steps in the diagnostics & therapeutics development pipelines and identify bottlenecks amenable to re-engineering
- Experiment with innovative methods to streamline the process
- Evaluate novel methods with compelling therapeutic projects



Examples of Translational Challenges

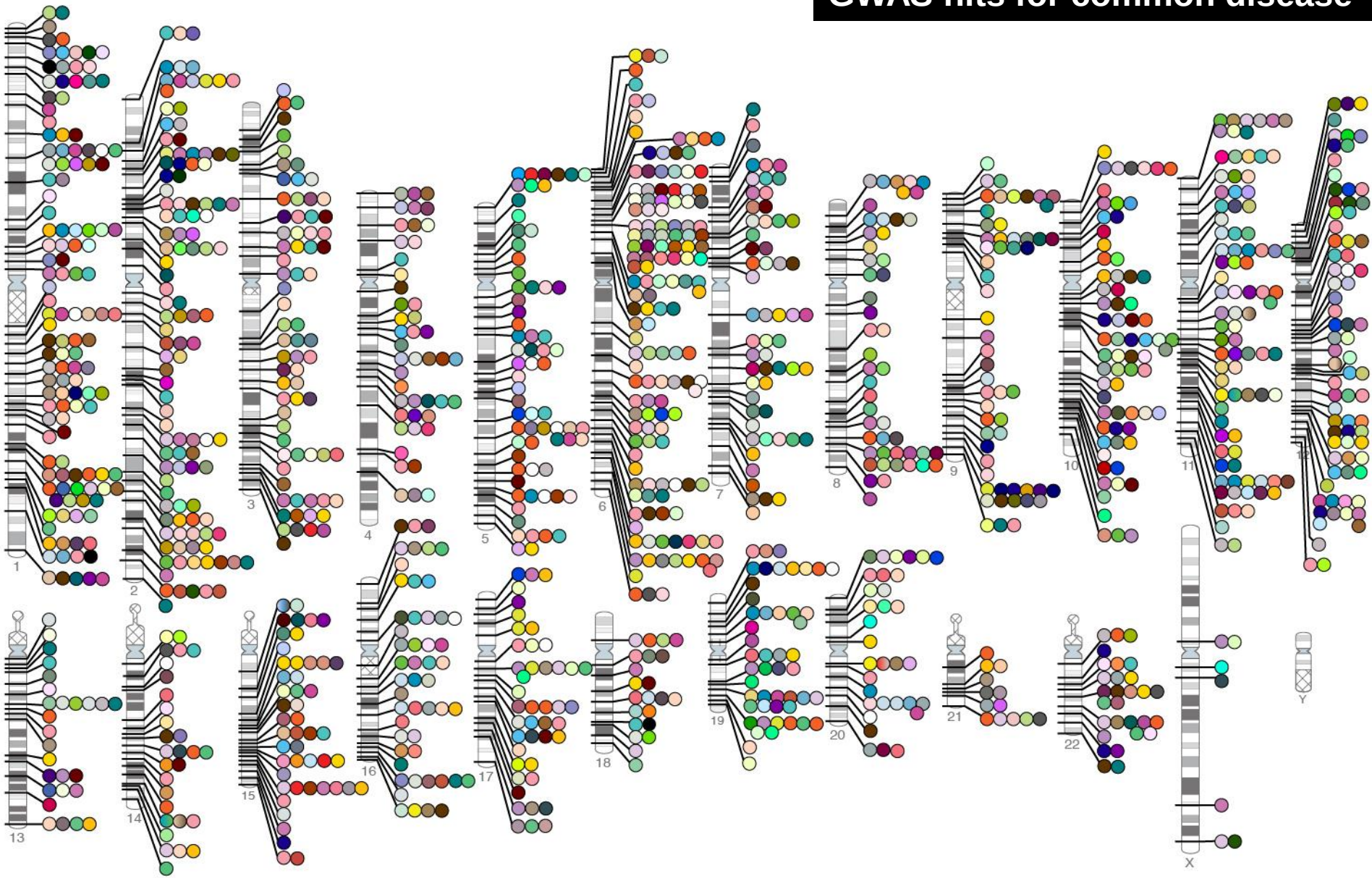
- Therapeutic target validation
- Chemistry
- Virtual drug design
- Preclinical toxicology
- Biomarkers
- Efficacy testing
- Phase zero clinical trials
- Rescuing and repurposing
- Clinical trial design
- Post-marketing research

Target Validation



Need new methods, approaches, tools, and technologies
to undertake validation in a
more efficient and predictable fashion

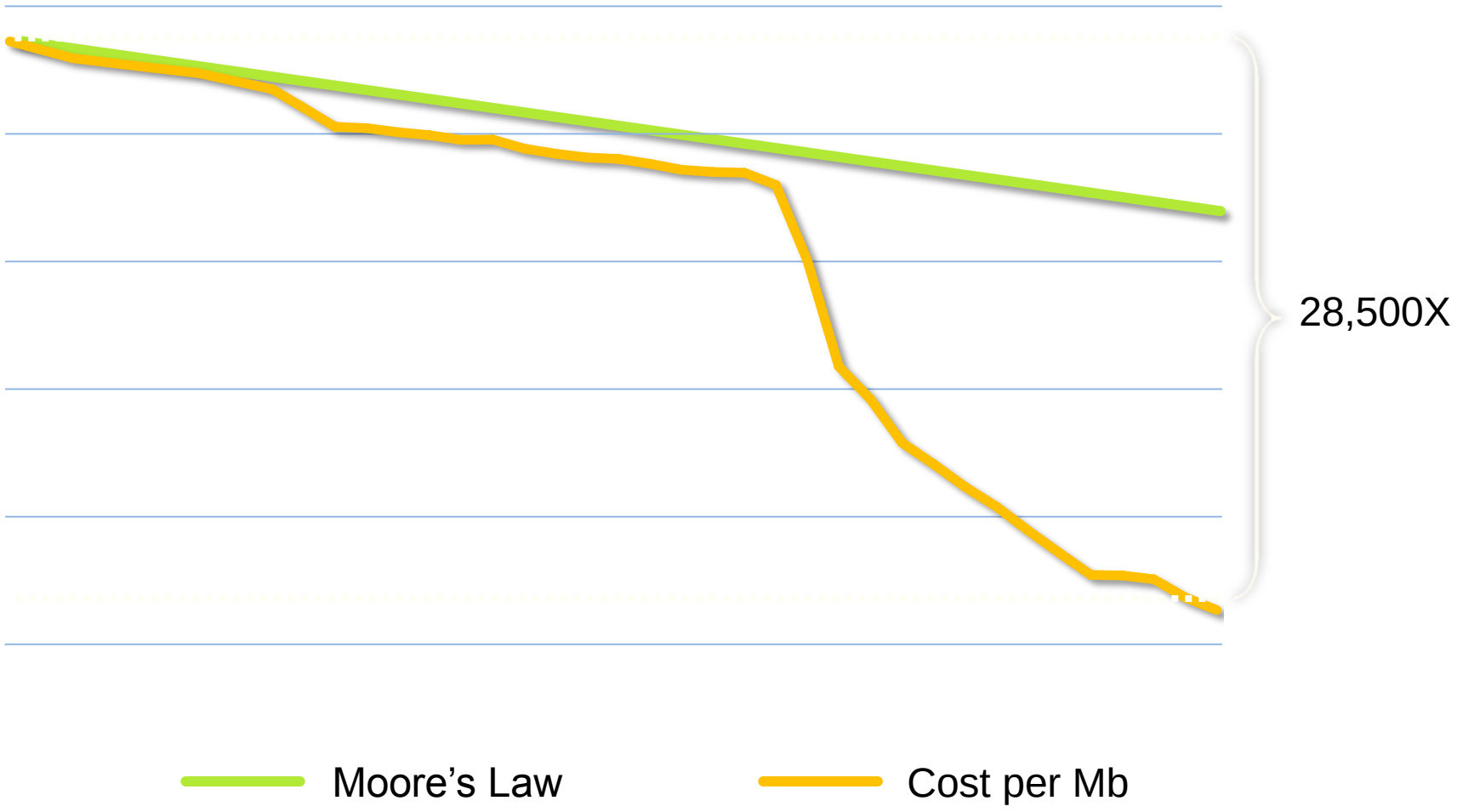
GWAS hits for common disease



“Positive controls” demonstrate power of GWAS to identify drug targets

Disease	Total GWAS hits	GWAS hits associated with marketed drugs
Type 2 diabetes	44	6
Hyperlipidemia	39	2
Multiple sclerosis	36	5
Psoriasis	24	4

Sequencing Costs Drop Faster than Moore's Law



Working Together: Target Validation NIH-Industry Workshop

Goal: to undertake target validation in a more systematic way

- Understand the landscape, including success and failures
- Develop new methods, approaches, tools, and technologies
- Capitalize on the wealth of new discoveries and resources

Next Steps: Standing Up a Target Validation Consortium

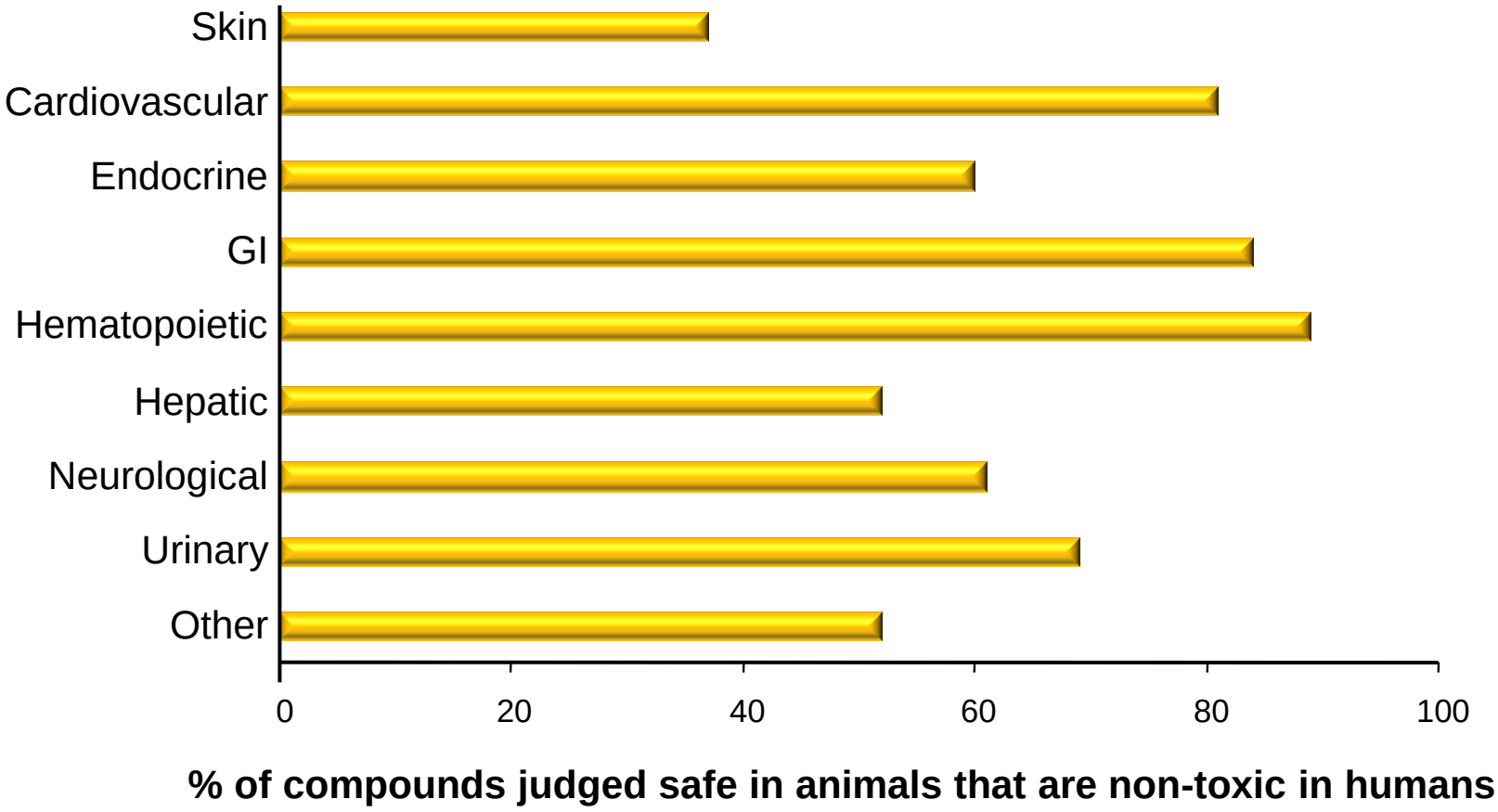
How is this different?

- Exceptional scientific opportunities
- Offers real change in the drug discovery paradigm
- Governance with high level involvement

Pre-Clinical Toxicity Testing

Constriction point: low concordance between animal and human toxicity

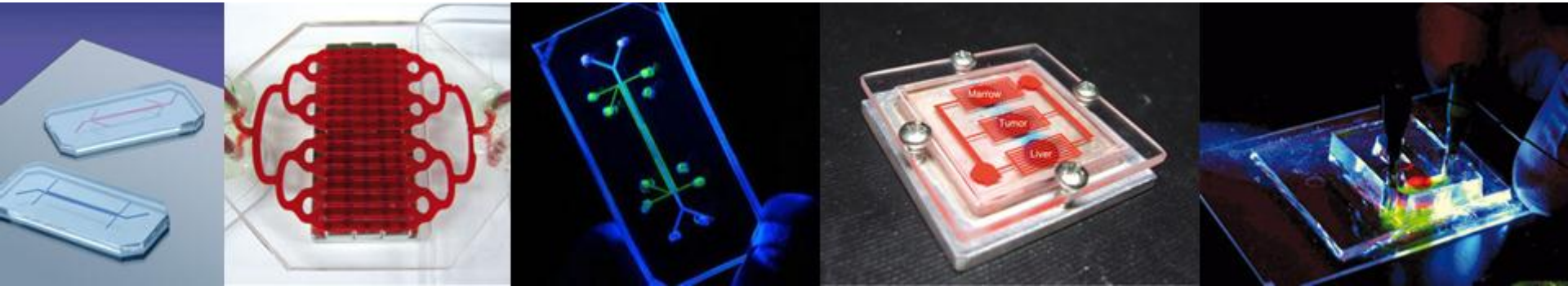
Preclinical (21%) + Clinical (12%) Tox = 33% of all failures (Kola and Landis, *Nature Reviews Drug Discovery* 3, 711-716, 2004)



Nature Reviews Drug Discovery 3, 227-236, 2004

Better Ways to Predict Drug Safety
New NIH-DARPA-FDA Collaboration

- Part of President's "Lab to Market" initiatives
- Goal: Develop chip to screen for safe, effective drugs
  - Liver, heart, lung, other cell types
  - Designed for multiple different readouts
- NIH, DARPA to commit ~$70 million each over 5 years
- FDA to offer guidance
- RFA published in mid-November; applications due January 26th
  - Seeking best ideas in engineering, biology, toxicology



Rescuing and Repurposing

NIH – INDUSTRY ROUNDTABLE

April 21–22, 2011

Exploring New Uses for Abandoned and Approved Therapeutics

NIH DRUG REPURPOSING

Drug	Initial Indication	Subsequent Indication
AZT	Antineoplastic	HIV/AIDS
Ceftriaxone	Bacterial infection	Amyotrophic lateral sclerosis
Hydroxyurea	Cancers	Sickle cell anemia
Metformin	Type 2 diabetes	Breast cancer
Pioglitazone	Type 2 diabetes	Hepatic steatosis
Raloxifene	Osteoporosis	Breast cancer
Tamoxifen	Breast cancer	Bipolar disorder

BIOMEDICINE

NIH's Seco

Although the U.S. Nati
Health (NIH) has made
posed new center aime
research, so far the main i
to put scattered existing p
same roof. But this mo
Francis Collins unveiled s
effort to persuade drug c
up their troves of abando
demics, who would look f

NIH DRUG

Drug
AZT
Ceftriaxone
Hydroxyurea
Metformin
Pioglitazone
Raloxifene
Tamoxifen

Double duty. NIH researchers have found new uses for several therapeutics.

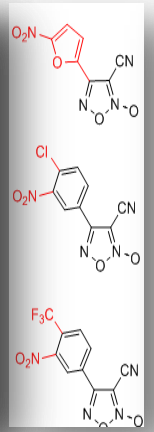
for repurposed drugs. And NIH says that

says. The drug rescue and repurposing project will be led by a team at NCATS as "an integral

Rescue and Repurposing

New NIH-pharma Collaboration

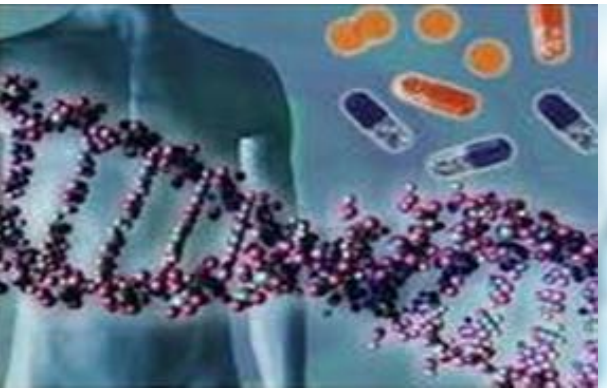
- Match compounds from pharma's "virtual medicine cabinet" with innovative ideas for new indications from NIH extramural scientists
- NIH provides: funding, RFA, review
- Pharma provides: compounds and pertinent data
- Terms are being worked out
- NIH-Industry working group – more partners following successful pilot?

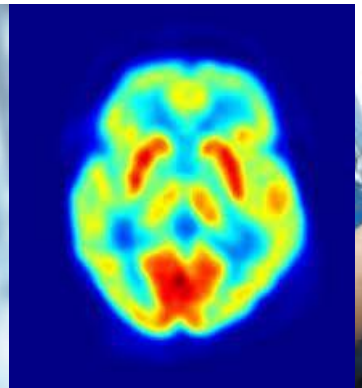


Disease | Target ID | Assay Dev. | HTS | Probe to Lead | Pre-Clinical | FDA IND | Ph. I | Ph. II | Ph. III | FDA Re-view | Clinic

Changing Human Subjects Research Landscape

- Human subjects regulations have not kept pace with changes in the human research enterprise:
  - Growth in research volume
  - Increase in multi-site studies
  - Increase in health services and social science research
  - New technologies: e.g., genomics, imaging, informatics
  - Increased role of private sector
  - Increased sharing of specimens and data






Revamping Human Subjects Protections: Enhancing Protections & Reducing Burden

- Advance Notice of Proposed Rulemaking (ANPRM) on Revisions to the Common Rule
- Issued by the Office of the Secretary in coordination with Office of Science and Technology Policy
- Interagency working group: representatives from NIH, FDA, HHS, OHRP, VA, OMB, OSTP

Regulatory Reform: Two Overarching Goals

1. Enhance protection of research subjects
2. Improve the efficiency of the review process by reducing:
   - Unnecessary paperwork
   - Multiple reviews of studies
   - IRB reviews of very low-risk research
   - IRB reviews of information risks

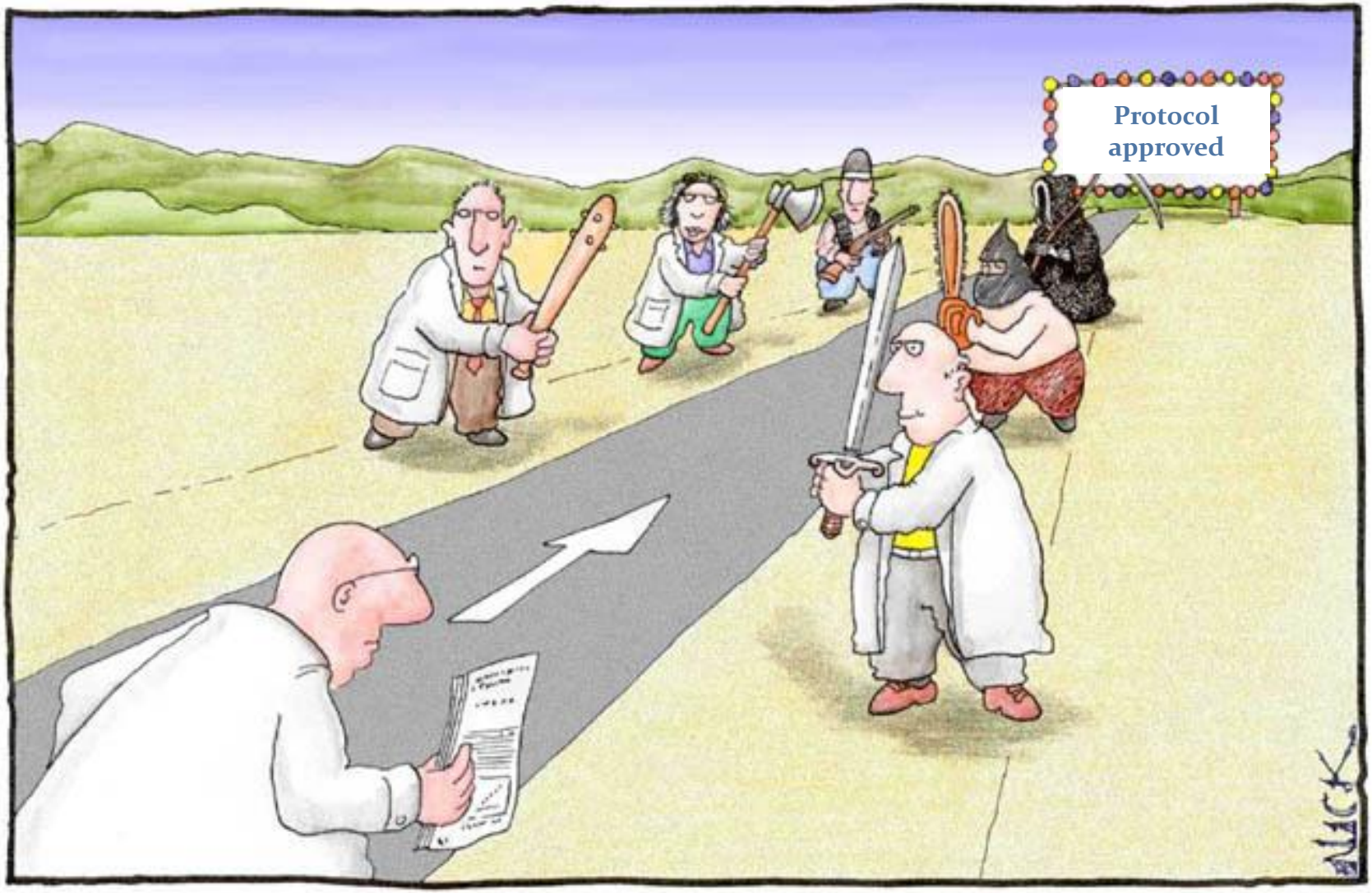
Seven Proposed Regulatory Reforms

1. Refine existing risk-based framework
2. Utilize single IRB review of record for domestic multi-site studies
3. Improve consent forms and consent process
4. Establish mandatory data security and information protection standards for studies involving identifiable or potentially identifiable data
5. Establish systematic approach to collection and analysis of data on unanticipated problems and adverse events
6. Extend federal regulatory protections to all research conducted at U.S. institutions receiving federal funding
7. Establish single source of guidance on federal regulations

Next steps for revision of Common Rule

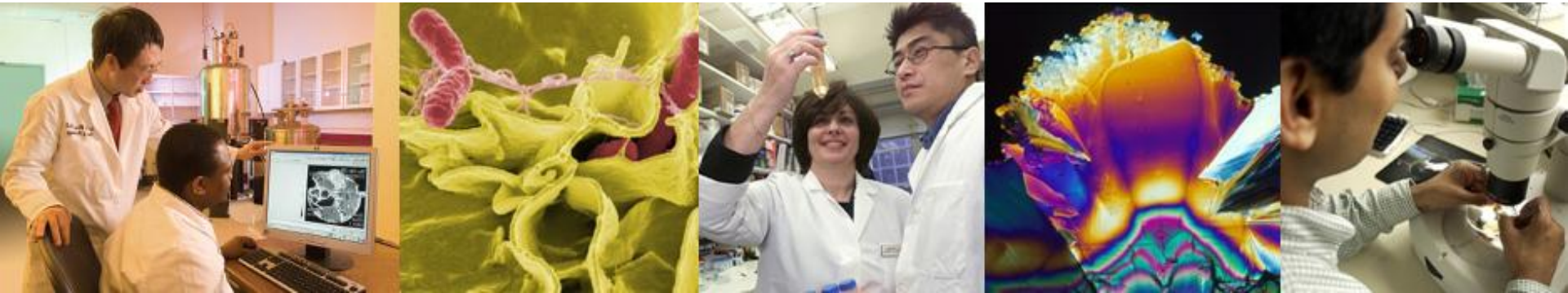
- Read and analyze public comments
- Publish draft revision – in the form of a notice of proposed rule making (NPRM) – early 2012
- Gather public comments on the NPRM
- Finalize regulation
- Assess impact on research participants and research progress

IRB Review: There has GOT to be a better way!

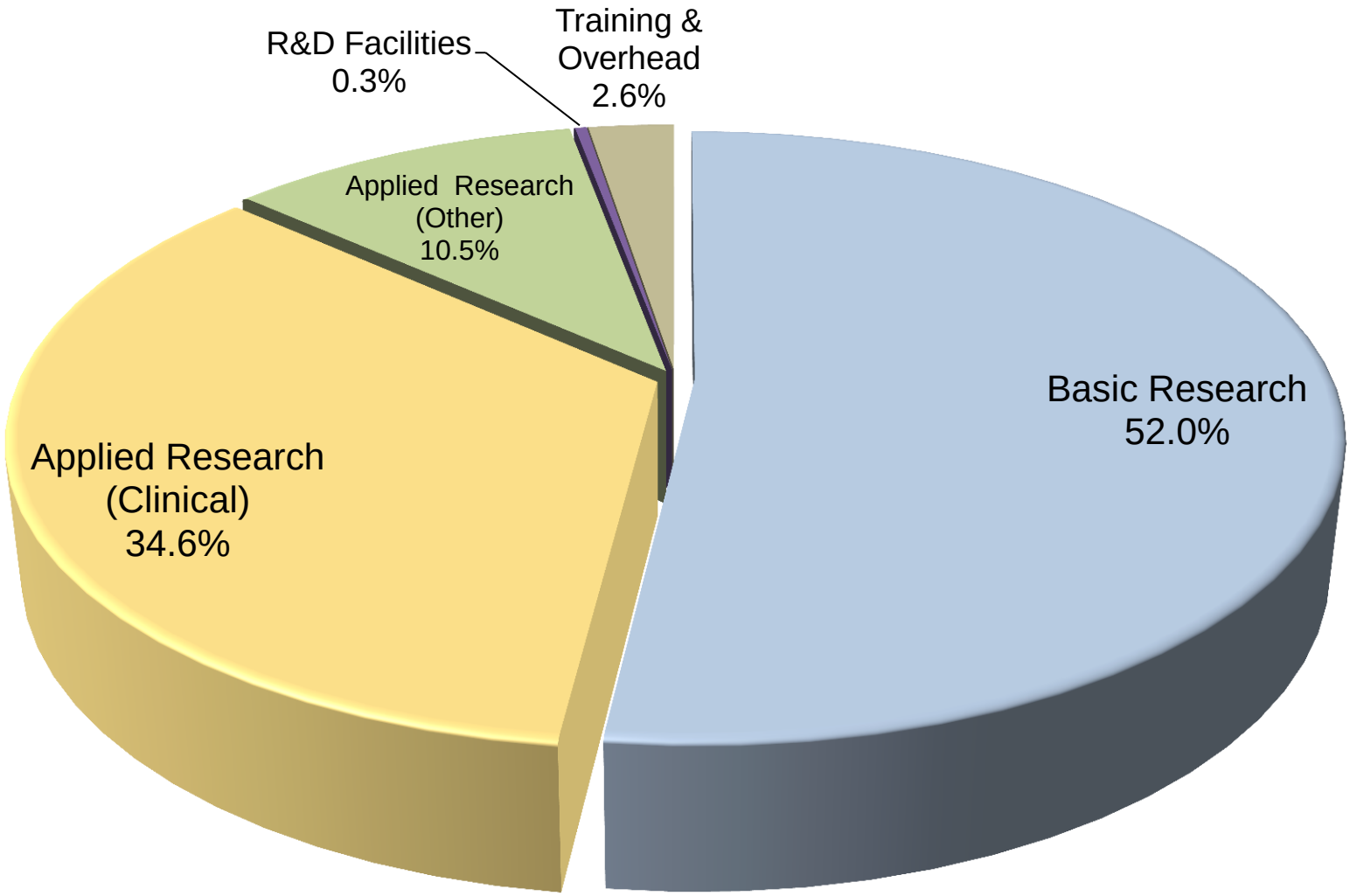


NCATS will:

- Facilitate – not duplicate – the translational research activities supported and conducted by the ICs
- Complement – not compete with – the private sector
- Reinforce – not reduce – NIH's commitment to basic science research



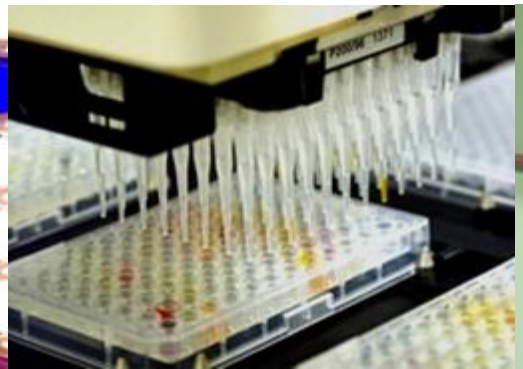
FY 2010 Percent Distribution of Basic and Clinical Research



NCATS Research Programs

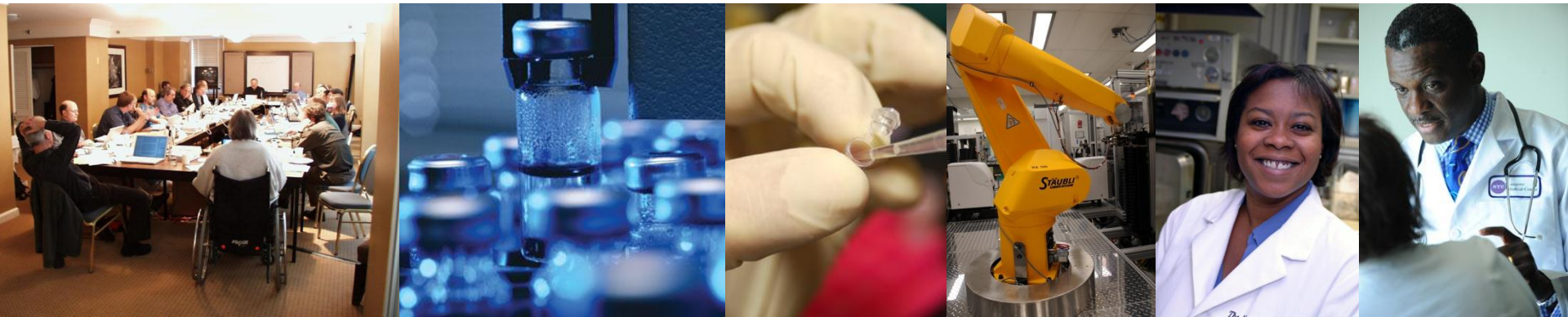
- Components of Molecular Libraries Program
- Therapeutics for Rare and Neglected Diseases
- Office of Rare Diseases Research
- Rapid Access to Interventional Development
- Clinical and Translational Science Awards
- FDA-NIH Regulatory Science
- Cures Acceleration Network






Cures Acceleration Network (CAN)

- Established by the Affordable Care Act
- Included in the Senate Report for FY12 at $20M
- CAN will advance the development of “high need cures” and reduce barriers between research discovery and clinical trials
- Funding flexibilities:
  - Large Grant Awards: Up to $15M per award per fiscal year
  - Partnership Awards: $1 for every $3 from NIH
  - Flexible Research Awards: DARPA-like authority



The ACD-NCATS Working Group

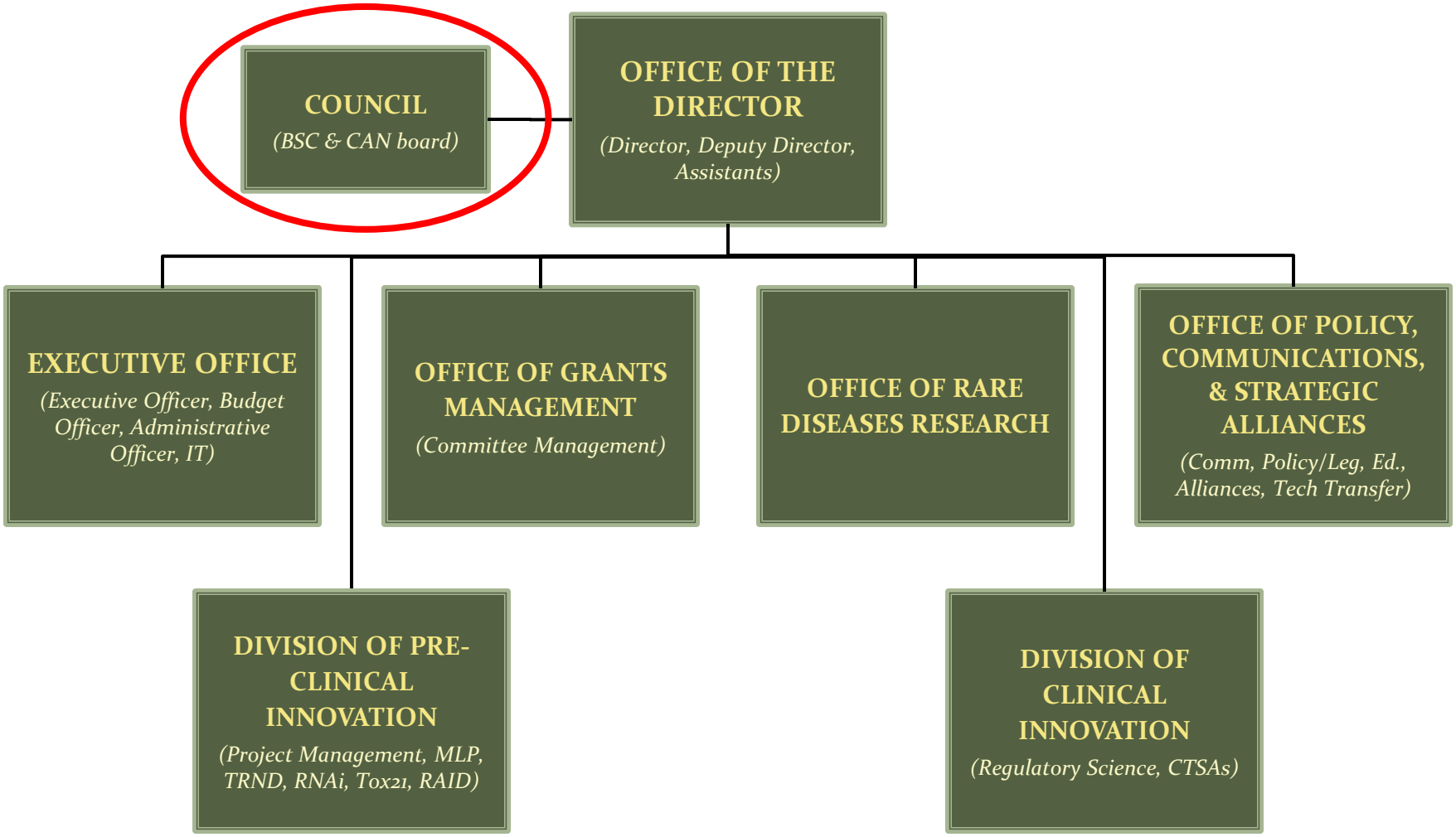
Provide high-level advice on the best ways that NCATS can speed the entire effort of getting effective medicines to patients.

- **Maria C. Freire, Ph.D.** ***(Chair)***
  Albert and Mary Lasker Foundation
- **Julian Adams, PhD**
  Infinity Pharmaceuticals, Inc.
- **Lee E. Babiss, PhD**
  Global Laboratory Services PPD, Inc.
- **Brook Byers, MBA**
  Kleiner Perkins Caufield & Byers
- **William W. Chin, MD**
  Harvard Medical School
- **Susan Desmond-Hellmann, MD**
  UCSF
- **David Ginsburg, MD**
  University of Michigan
- **Victoria Hale, PhD**
  Medicines360
- **Helen H. Hobbs, MD**
  University of Texas at Southwestern
- **Robert S. Langer, ScD**
  Massachusetts Institute of Technology
- **Stelios Papadopoulos, PhD**
  Exelixis
- **Mary K. Pendergast, JD**
  Pendergast Consulting
- **Moncef Slaoui, PhD**
  GlaxoSmithKline
- **Marc Tessier-Lavigne, PhD**
  Genentech, Inc.
- **David L. Valle, MD**
  Johns Hopkins

ACD-NCATS Report Findings
NCATS Can:

- Catalyze translation by promoting innovative research
- Galvanize and support new partnerships
- Support and augment the discipline of regulatory science and its application
- Expand the precompetitive space
- Harness the power of the CTSA Program
- Transformation through training
- Streamline administrative processes

NCATS Organization

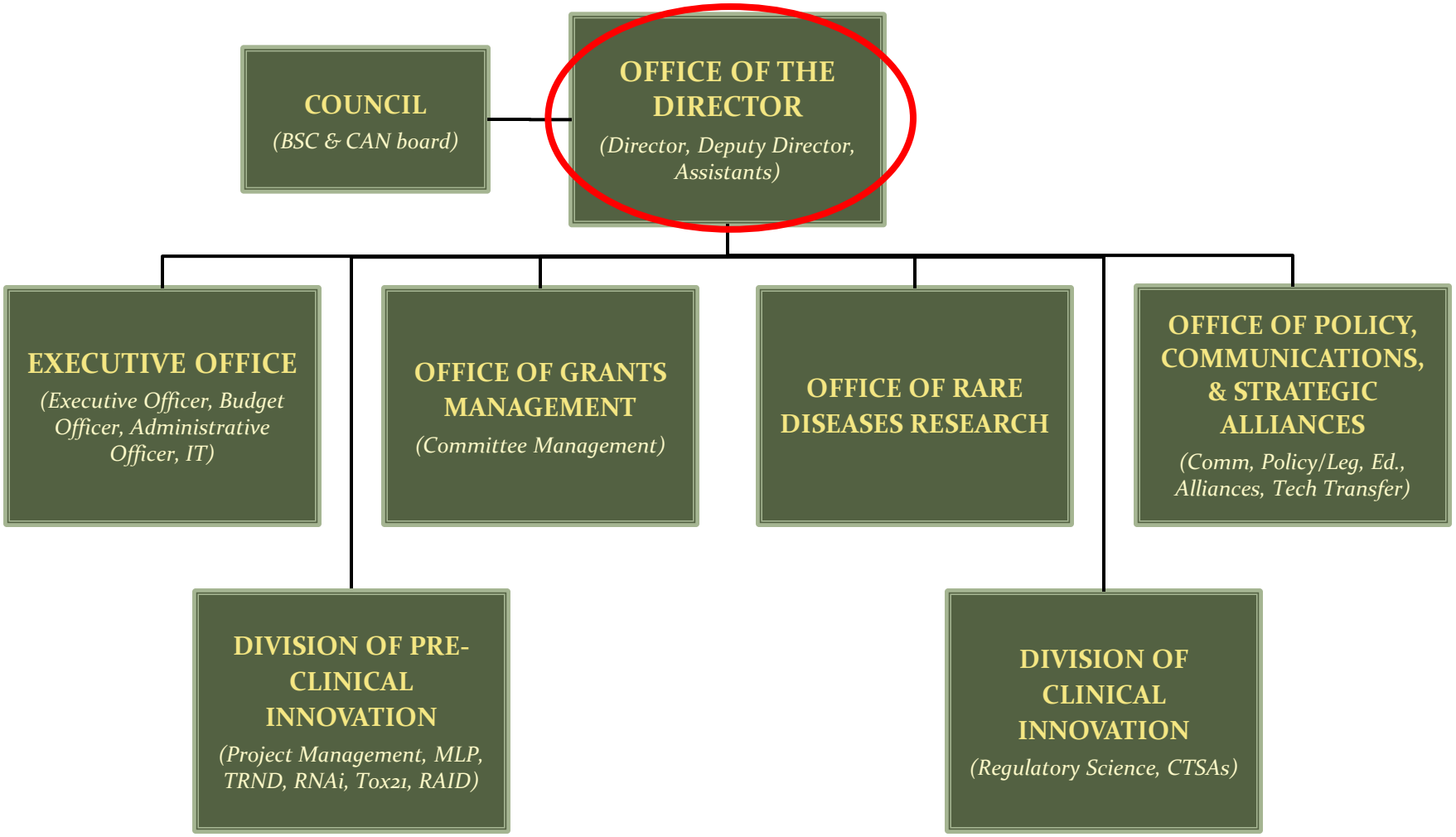


CAN Board (and NCATS Council and BSC)

Voting members	
Venture Capitalist	4 Individuals
Disease Advocate	8 Individuals
Basic research	
Medicine	
Biopharmaceuticals	
Discovery and delivery of medical products	
Bioinformatics and gene therapy	
Medical instrumentation	
Regulatory review	
Not specified	5 Individuals

Non-Voting members
National Institutes of Health
Food and Drug Administration
Office of the Assistant Secretary of Defense for Health Affairs
National Science Foundation
Veteran's Health Administration

NCATS Organization



NCATS Director: Search Committee

Co-chairs: Eric Green and Tom Insel

Members:

- NIH: Anthony Fauci and Story Landis
- Margaret Anderson, FasterCures
- Amy Comstock-Rick, Parkinson's Action Network
- Geoff Duyk, TPG Biotech
- Freda Lewis-Hall, Pfizer
- Brad Margus, Envoy Therapeutics
- Steven Marc Paul, Weill Cornell Medical College
- Marc Tessier-Lavigne, Rockefeller University
- Janet Woodcock, FDA

NCATS Director

He or she must…

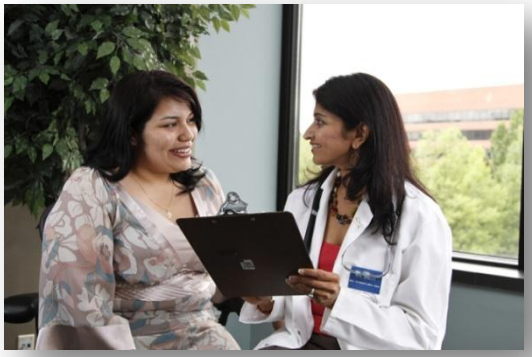
- Have expertise that transcends a single discipline
- Have experience in academia and the private sector
- Be able to convene diverse partners
- Be willing to engage in “disruptive innovation”

The Innovation Imperative ...

I have a great respect for incremental improvement, and I've done that sort of thing in my life, but I've always been attracted to the more revolutionary changes. I don't know why. Because they're harder. They're much more stressful emotionally. And you usually go through a period where everybody tells you that you've completely failed.

Steve Jobs

Tell Us What You Think

NIH...

Turning Discovery Into Health