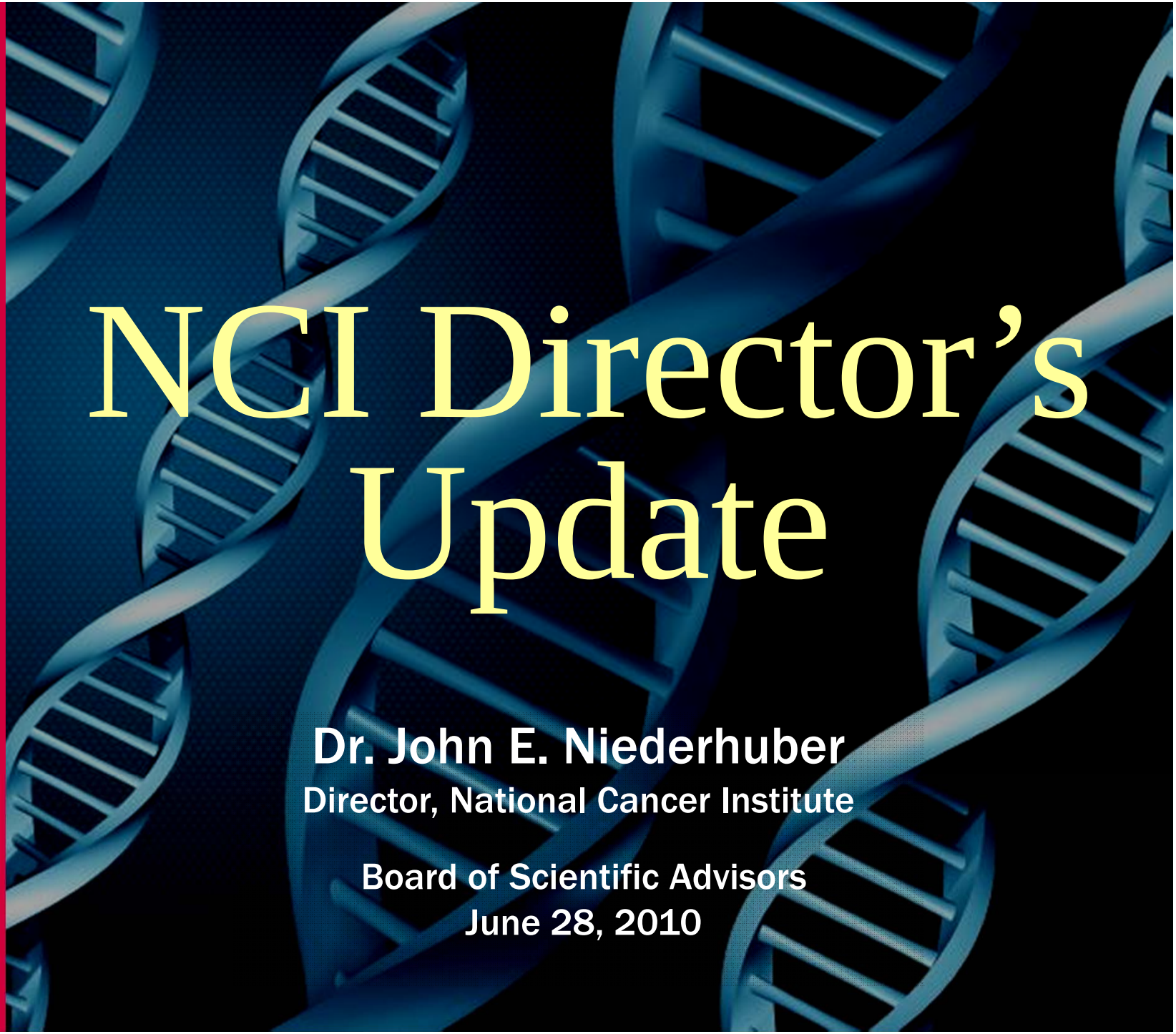
National Cancer Institute



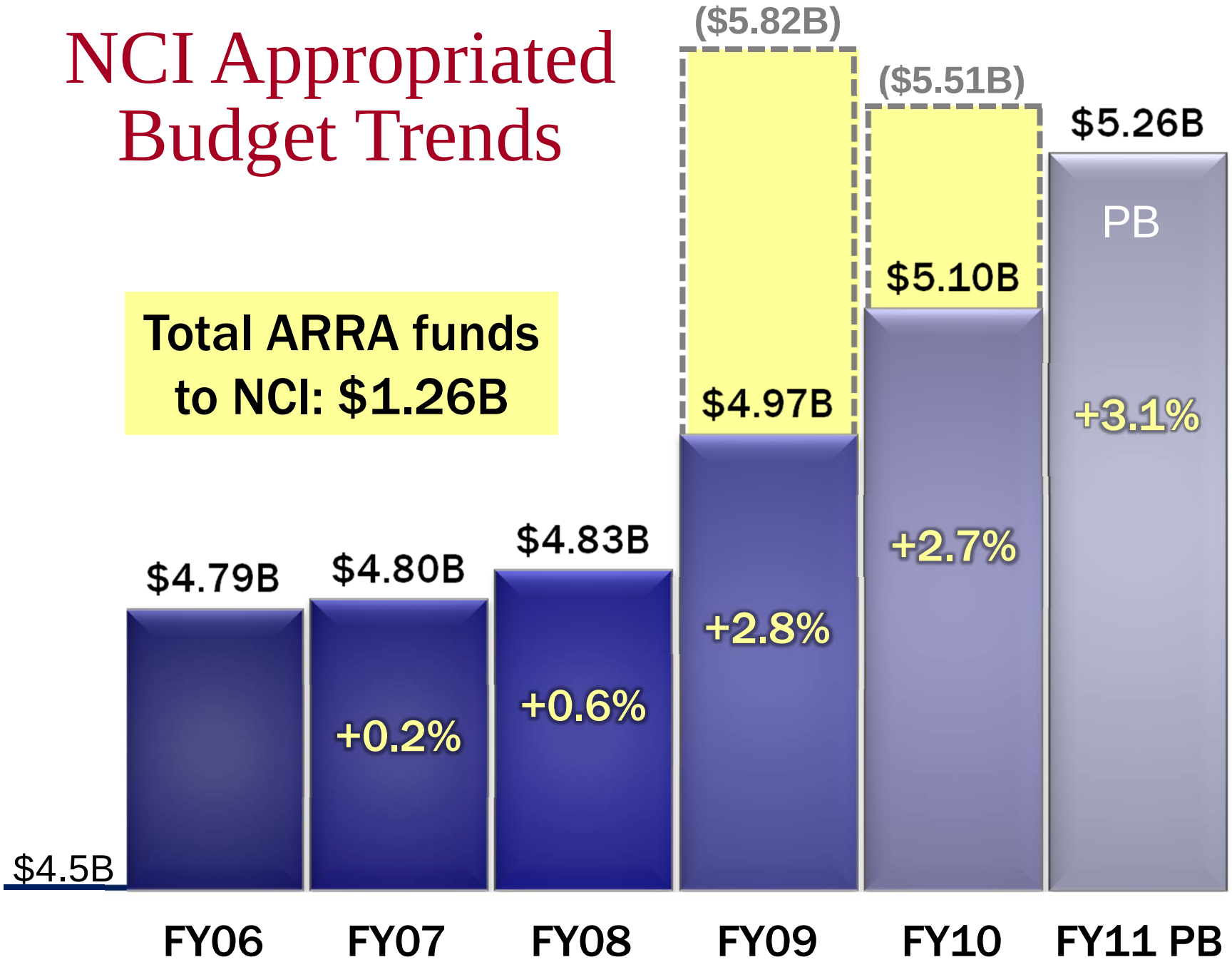
NCI Director's Update

Dr. John E. Niederhuber
Director, National Cancer Institute

Board of Scientific Advisors
June 28, 2010

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

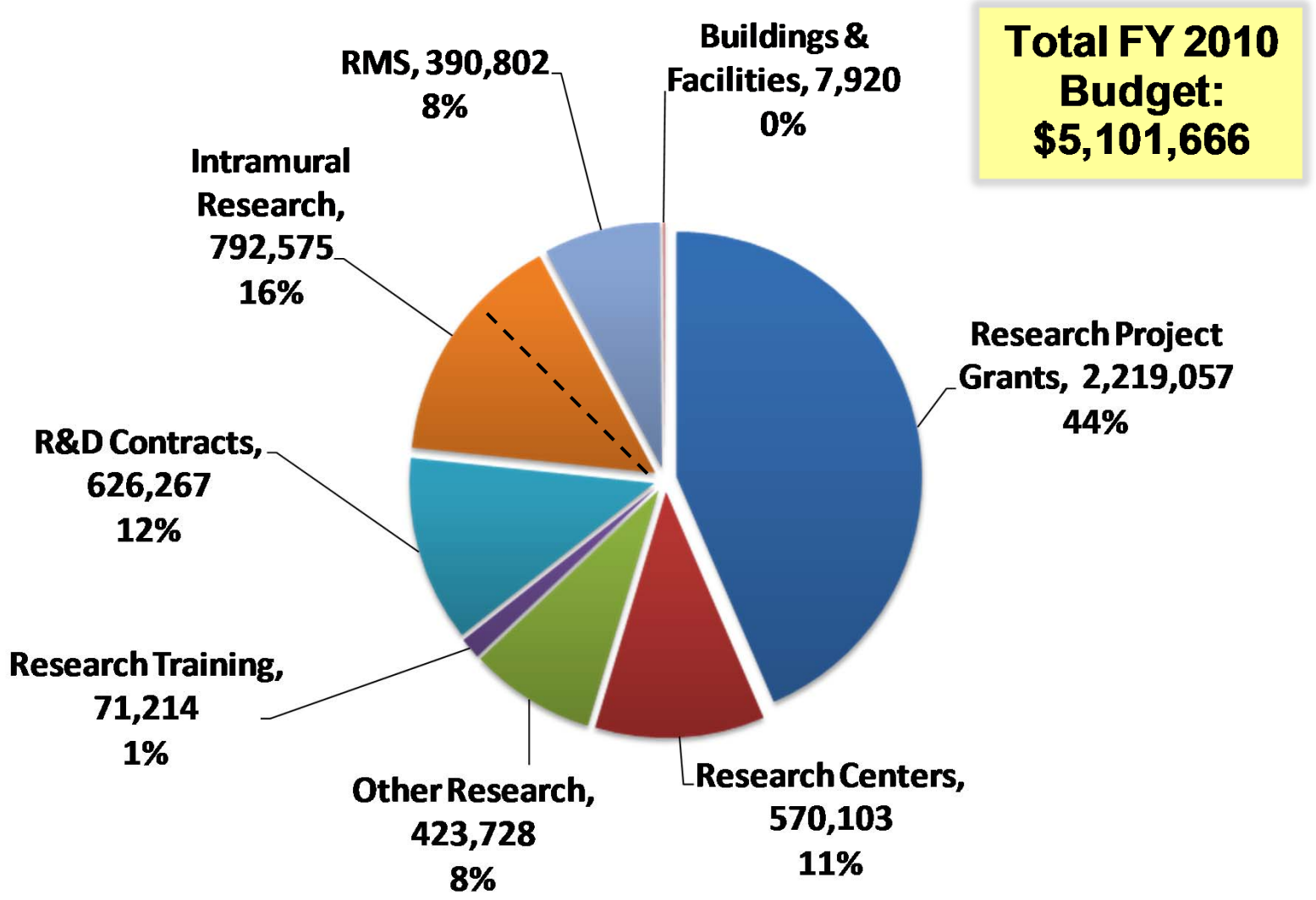
NCI Appropriated Budget Trends



Applications for 2011

- FY11 President's Budget estimate (without ARRA bump)
  - 1,220 competing RPG awards
  - ~7,300 estimated applications
  - 16.8% success rate
- Estimating ARRA bump in applications
  - 400 GO and Challenge Grants unfunded
  - 106 ARRA 2-year R01s funded
  - ~7,800 possible applications (↑~500)
  - 15.7 % success rate

NCI FY 2010 Budget by Mechanism



(dollars in thousands)

Preparing for the Fourth Quarter of FY 2010

- **FY 2010 is on track to close out, as expected — without major issues**
  - **Approaching the fourth quarter,** about 60 percent of the NCI research budget has been obligated
    - **This is slightly ahead of where we were at this time last year**

Preparing for the Fourth Quarter of FY 2010

- FY 2010 is on track to close out, as expected
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- NCI's Executive Committee continues to prioritize funding decisions within budget constraints
- Weekly budget meetings track spending and keep NCI on track for a balanced budget at year's end
- EC traditionally holds a summer budget retreat; holding dates for new director

Preparing for the Fourth Quarter of FY 2010

- **Current estimate for FY 2010 competing RPGs is $496 million**
  - **Nearly $40 million more than projected for FY 2010**
    - Payline = 15th percentile
- **We have set aside $203 million for RFAs, which is $70 million more than last year**

Planning NCI's space needs for the years ahead.

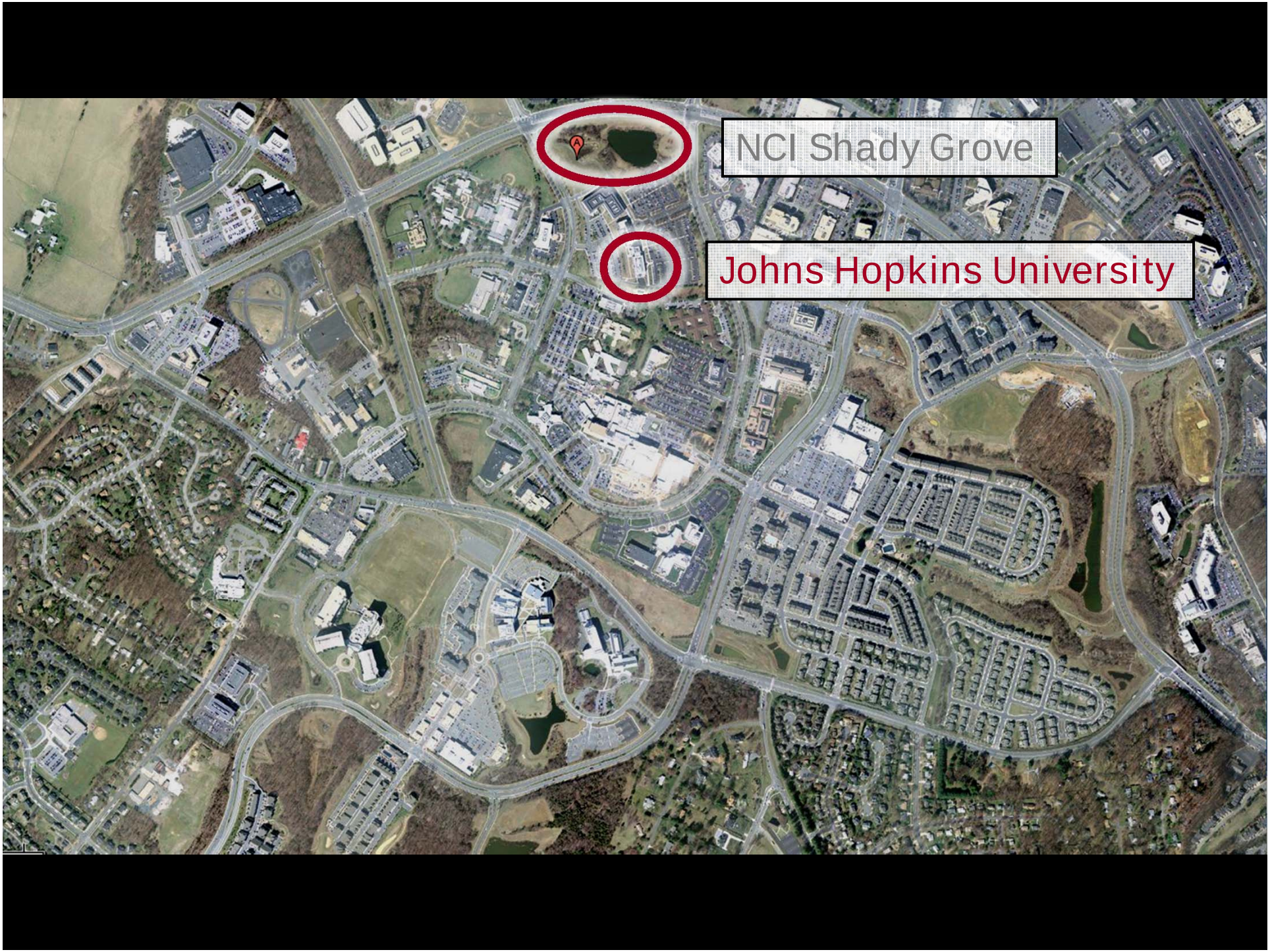
Executive Plaza

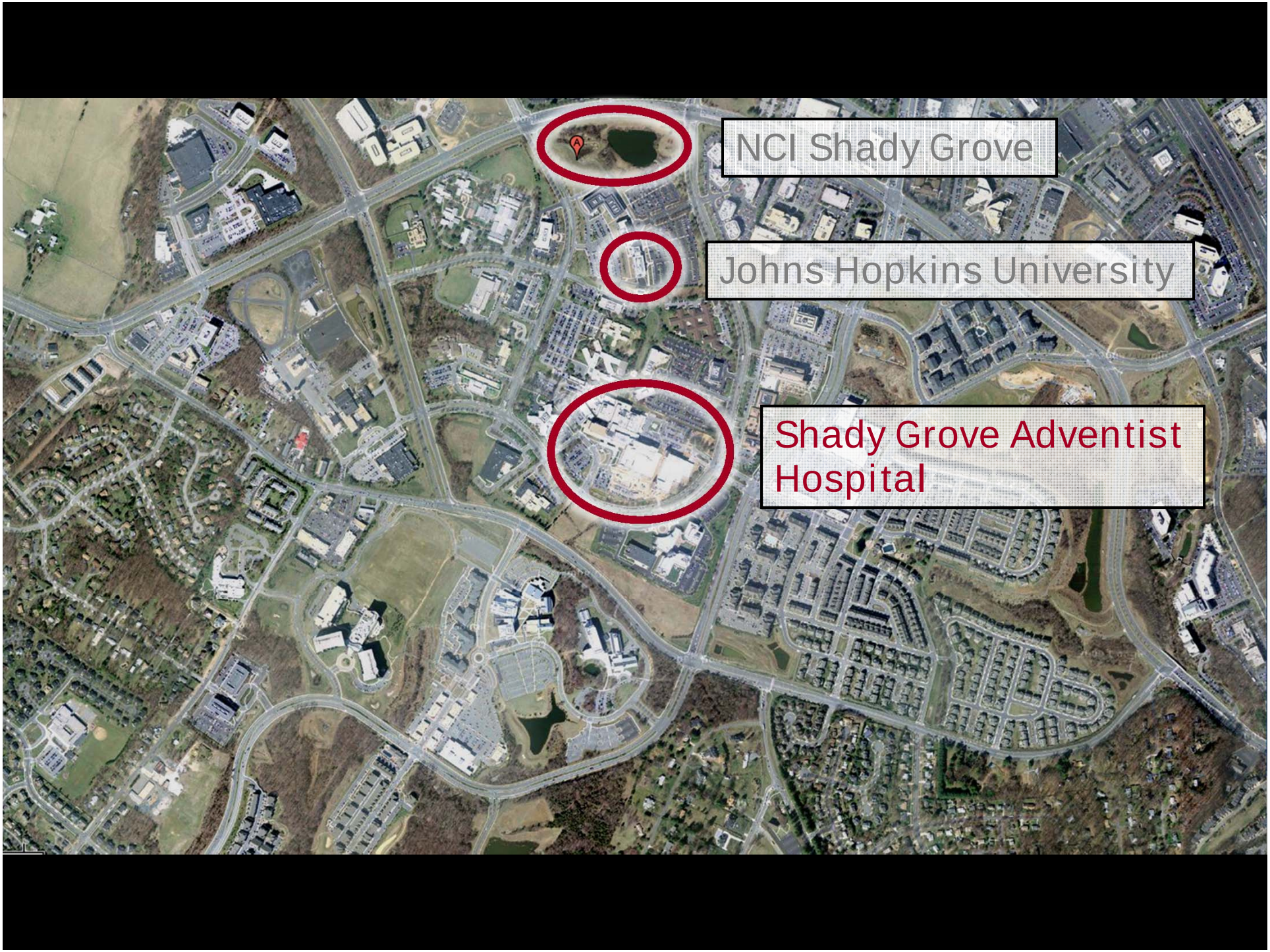
NCI Shady Grove

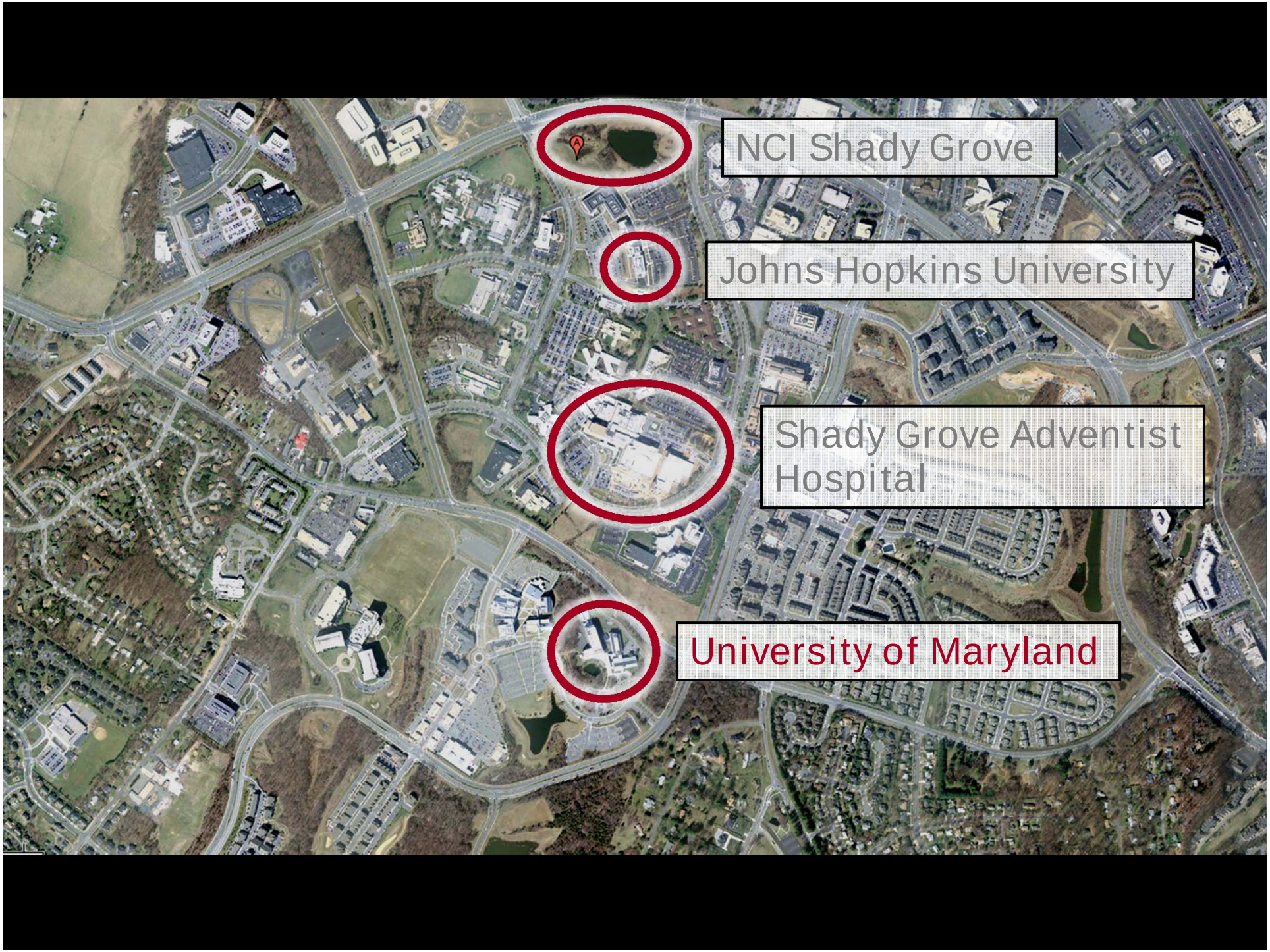
Selected after a rigorous, year long competitive bidding process conducted by the General Services Administration, in consultation with NIH and NCI

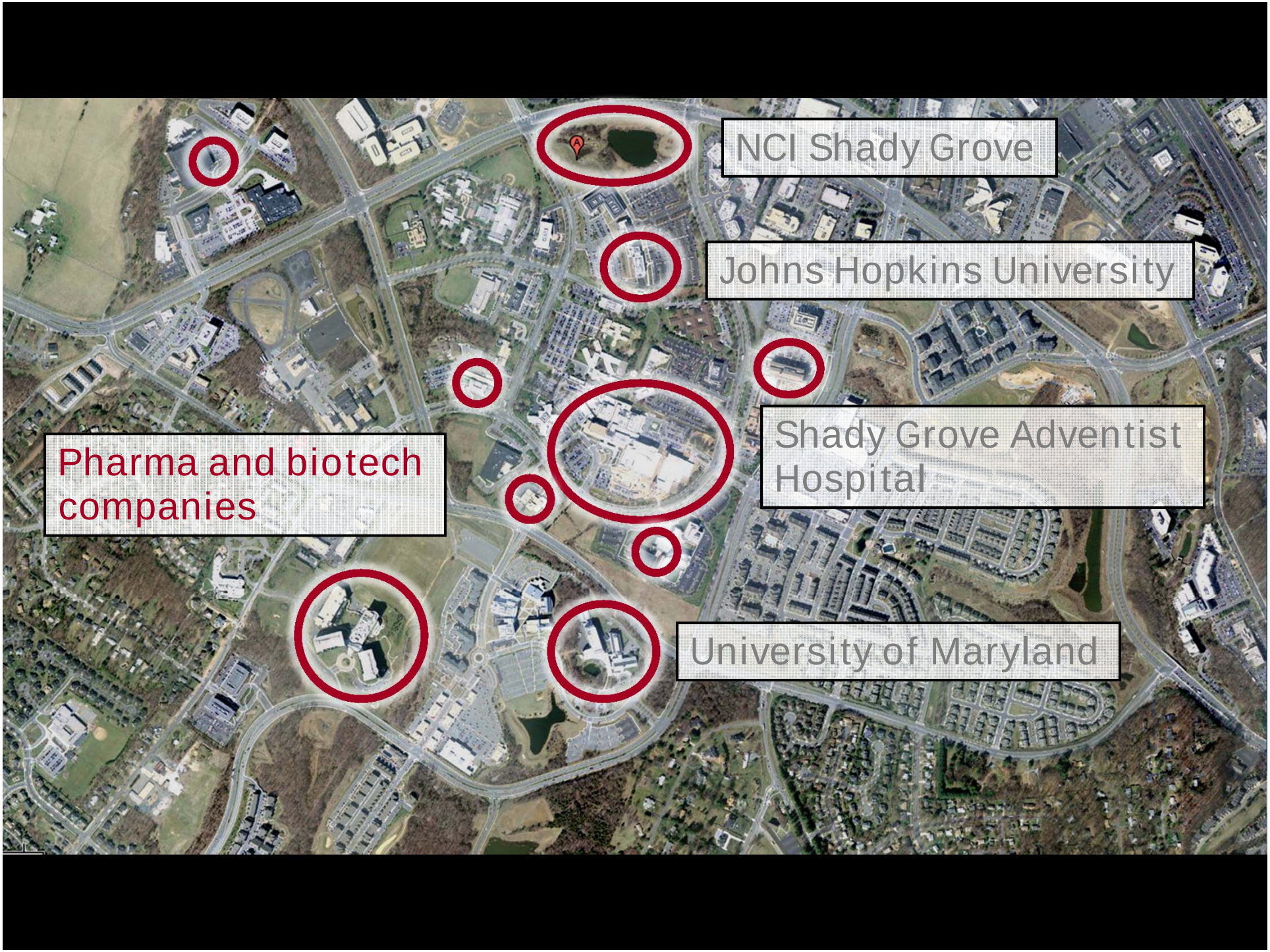
- 2 new custom-built, state-of-the-art buildings with 490,000 net square feet of usable space
- Able to accommodate ~2,400 staff members
- Leadership in Energy & Environmental Design (LEED) Silver Rating
- Move will take place in early 2013


NCI Shady Grove


NCI Shady Grove
Johns Hopkins University


NCI Shady Grove
Johns Hopkins University
Shady Grove Adventist Hospital


NCI Shady Grove
Johns Hopkins University
Shady Grove Adventist Hospital
University of Maryland


NCI Shady Grove
Johns Hopkins University
Shady Grove Adventist Hospital
Pharma and biotech companies
University of Maryland

Meeting the increasing need for public-private partnerships.

NCI-Frederick, Bldg. 549

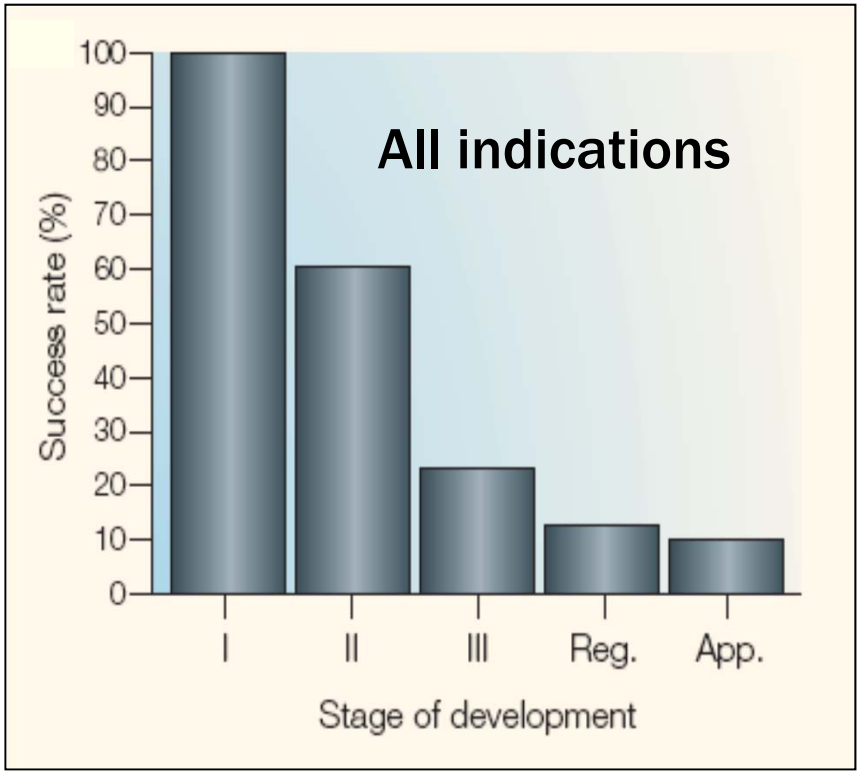
Advanced Technology Research Facility

- 330,000 square foot facility will contain:
  - NCI's Biopharmaceutical Development Program manufacturing facility
  - **NCI's Advanced Technology Program**
  - **Advanced Computing Program**
  - **Incubator Space for Initial Private Partnerships**

Advanced Technology Research Facility

Presented the 2010 Economic Development Award by the Maryland Economic Development Association

Most Drugs Fail in Late Stages of Development, Particularly in Oncology

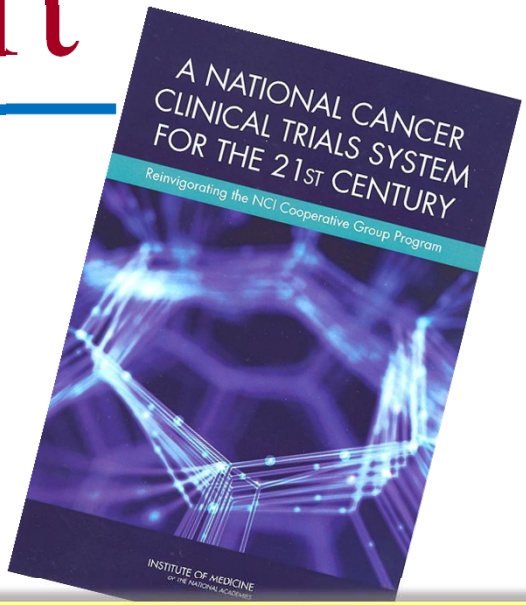


Rates of success for compounds entering first-in-man that progress to subsequent phase trials

- 70% of oncology drugs that enter Phase 2 fail to enter Phase 3
- 59% of oncology drugs that enter Phase 3 fail
- Late stage failure leads to enormous risk
- Failure is more often due to lack of efficacy than to toxicity

Kola & Landis; Nature Reviews Drug Discovery 2004

IOM Report

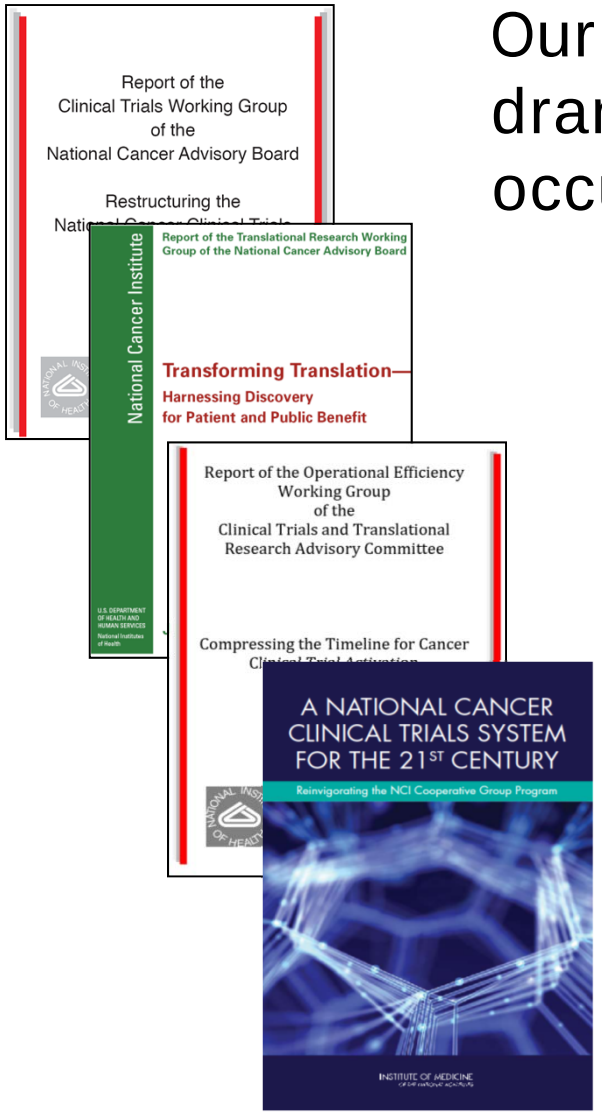


- "A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program"
  - **Co-chairs: John Mendelsohn and Harold L.**
  - **"With many la trials system cumbersome needs to be re and improve move beyond academic, go**

Four goals:

- **Promote consolidation and efficiency**
- **Incorporate innovation in science and trial design**
- **Provide adequate funding and support**
- **Incentivize participation by patients and physicians**

Changing the NCI's Clinical Trials System to Meet the Needs of the 21st Century



Our clinical trials system must reflect dramatic changes in cancer biology that occurred over the past 15-20 years

What do we need to change?

- **Improve the speed and efficiency of the development and conduct of trials**
- **Incorporate innovative science and trial design into our studies**
- **Improve prioritization, support, and completion of trials**
- **Incentivize the participation of patients and physicians in clinical investigations**

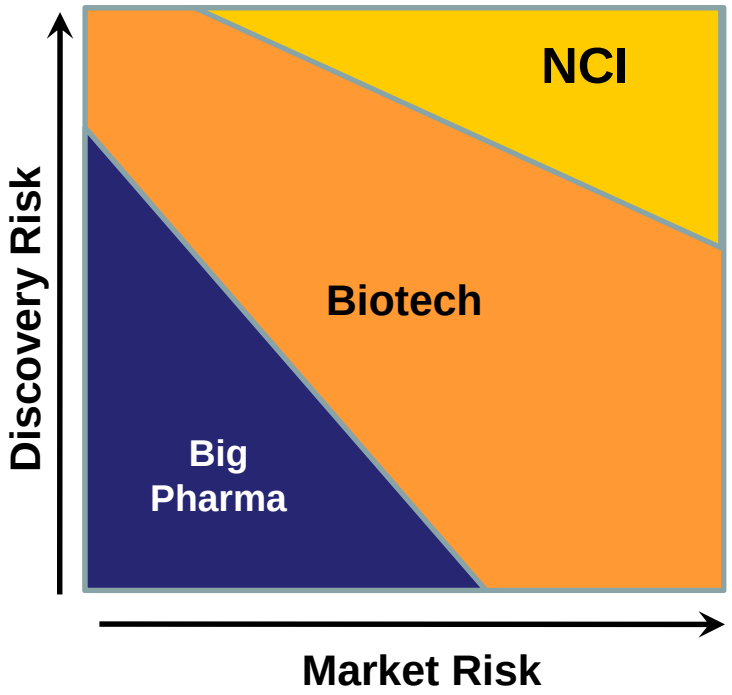
What have we changed?

- **Resources for the development of predictive biomarkers**
- **Clinical trial prioritization**
- **Operational efficiency standards for trial development**
- **Regulatory & administrative support**
- **Modernized clinical trial IT infrastructure**

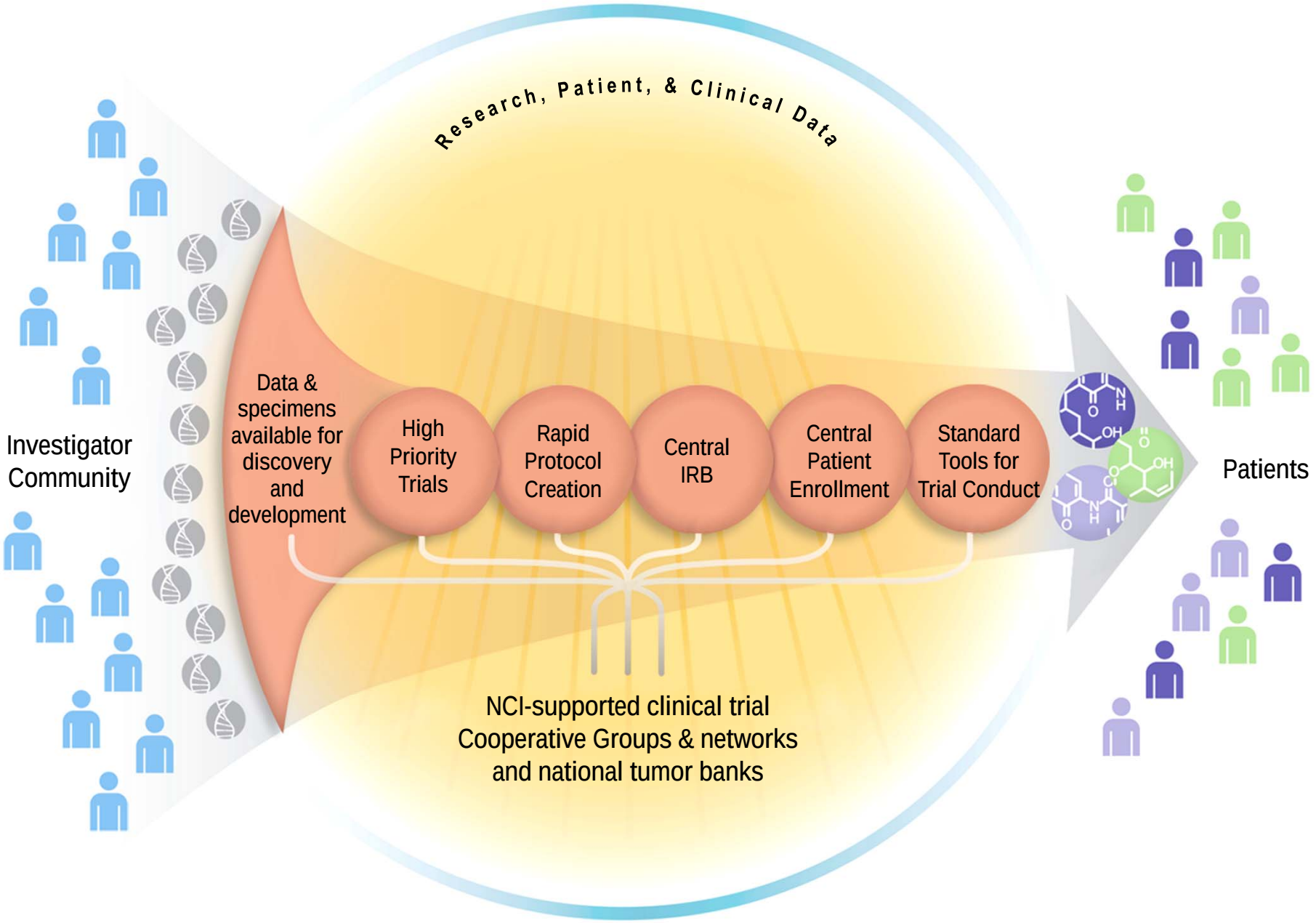
Where do we go from here?

NCI's Vision for Drug Development

- Implementing the "Dilts study" data to achieve clinical trial efficiencies
- Not intended to replicate Pharma
- Focus on bringing academic targets and molecules to patients
- Will not shy away from difficult targets
- Longer time horizon
- Valley of Death – mitigating risk
- Pre-clinical research infrastructure for early "go-no go" decisions



NCI National Clinical Trials System



NExT Program

Merger of NCI drug and imaging agent development programs

- **Integration of PD-Biomarkers Program**
- **Creation of** Chemical Biology Consortium
- **Development of** Functional Biology Consortium

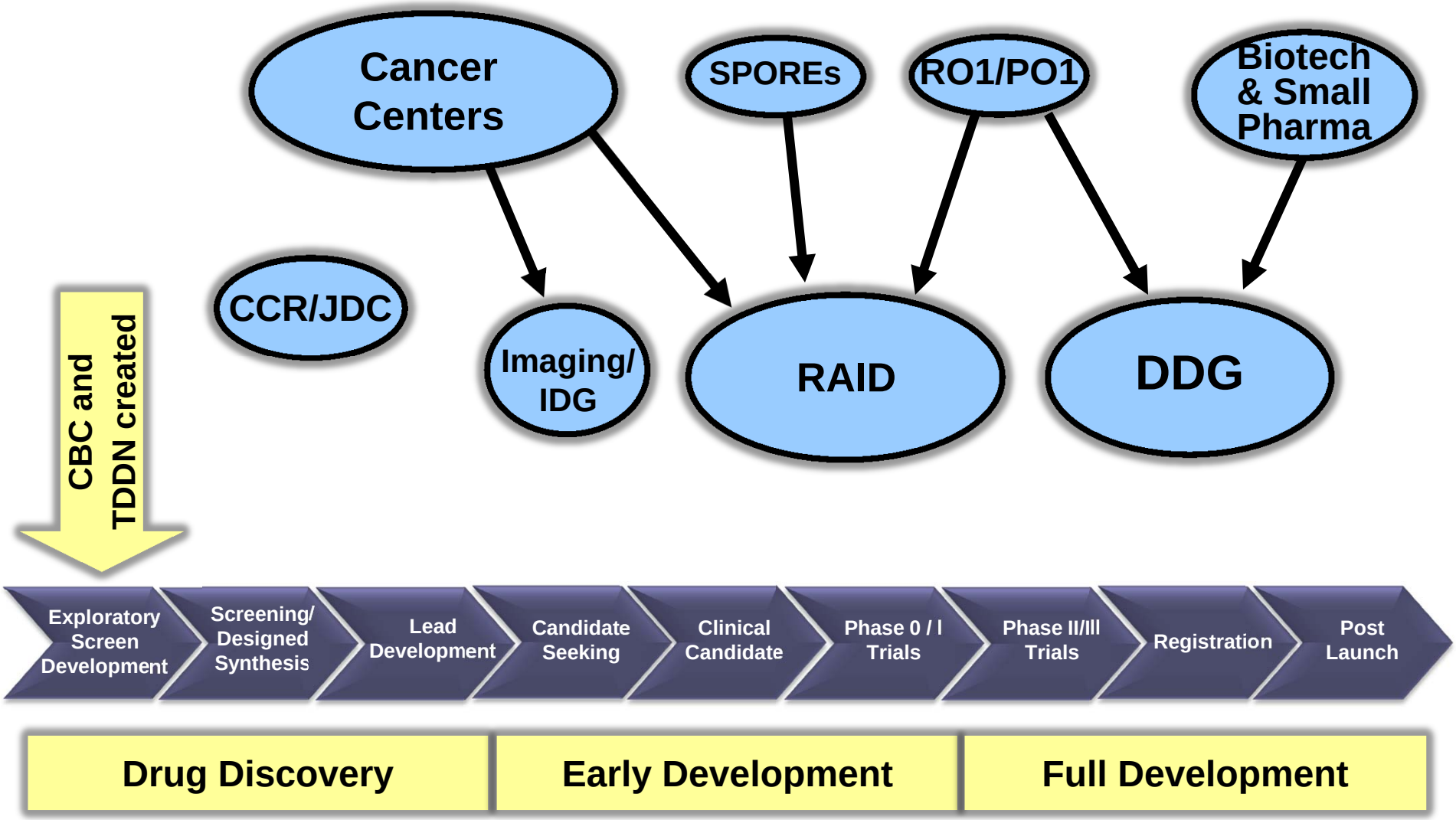
Mission of the NCI Experimental Therapeutics (NExT) Program

"To advance clinical practice and bring improved therapies to patients with cancer by supporting the most promising new drug discovery and development projects."

"The NCI will partner with successful applicants to facilitate the milestone-driven progression of new anti-cancer drugs (small molecules, biologics) and imaging agents towards clinical evaluation and registration."

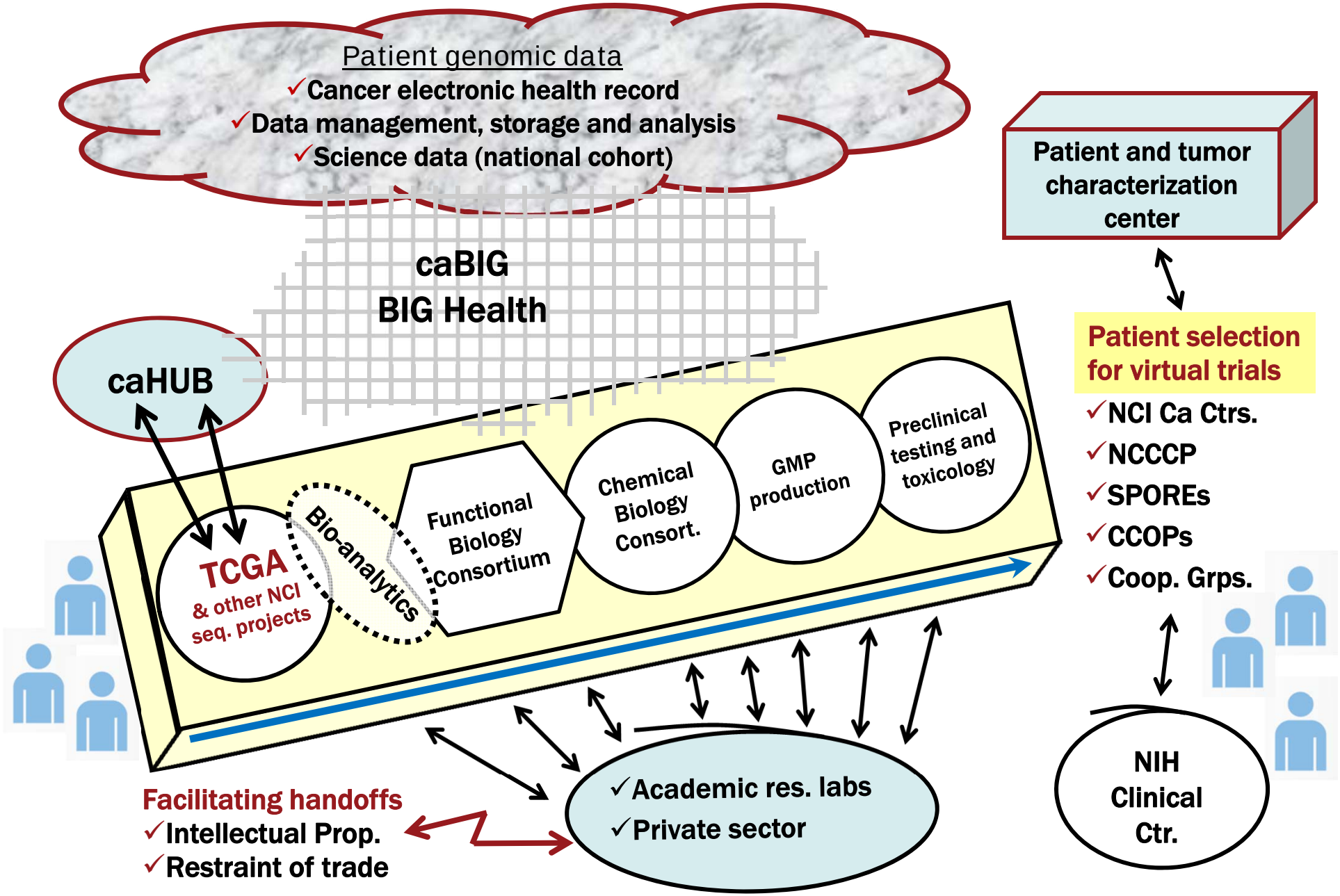
http://next.cancer.gov

The NExT Pipeline



NExT Application and Review Process

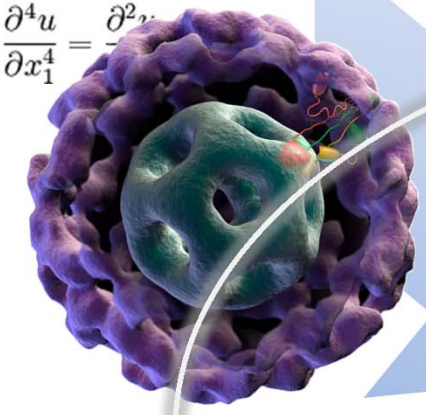
- 4 rounds annually; completed review of 3 cycles
- Cycle one: 52 applications received
  - Discovery: 44 applications; 8 approved
  - Development: 8 applications; 2 approved
- Cycle two NExT & RAID: 53 applications
  - Discovery: 20 applications, 3 approved
  - Development: 33 applications, 6 approved
- Cycle three NExT: 23 applications
  - Discovery: 11 applications, 3 approved
  - Development: 12 applications, 3 approved


Patient genomic data
✓Cancer electronic health record
✓Data management, storage and analysis
✓Science data (national cohort)
caBIG
BIG Health
caHUB
TCGA
& other NCI seq. projects
Bio-analytics
Functional Biology Consortium
Chemical Biology Consort.
GMP production
Preclinical testing and toxicology
Patient and tumor characterization center
Patient selection for virtual trials
✓NCI Ca Ctrs.
✓NCCCP
✓SPOREs
✓CCOPs
✓Coop. Grps.
NIH Clinical Ctr.
✓Academic res. labs
✓Private sector
Facilitating handoffs
✓Intellectual Prop.
✓Restraint of trade


EC Scientific Retreat
"Making Personalized Cancer Medicine a Reality What Will It Take?"
Clinical annotation is key
http://www.cancer.gov/directorscorner

Computational biology/
subcellular imaging

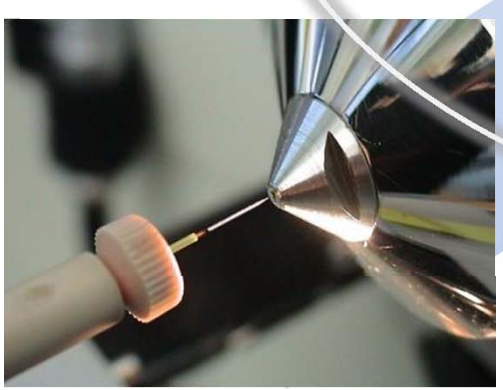
$$,_2 \Leftrightarrow \frac{\partial u}{\partial t} = \frac{\partial u}{\partial x_1} + \frac{\partial u}{\partial x_2}$$
$$0 \Leftrightarrow \frac{\partial^2 u}{\partial x_1^2} + \frac{\partial^2 u}{\partial x_2^2} + \frac{\partial^2 u}{\partial x_3^2} = 0$$
$$u \Leftrightarrow \frac{\partial^4 u}{\partial x_1^4} = \frac{\partial^2}{}$$



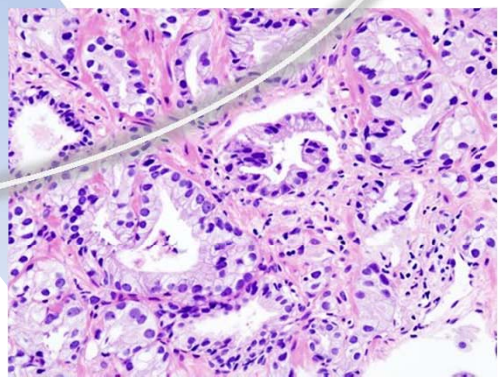
Somatic epi/genomics

Germline susceptibility
(C-GEMS,
pharmacogenomics)

Integration – from discovery to therapy



Proteomics
Functional biology



Phenotypes

Messages from the EC Scientific Retreat

- Cancer must be analyzed as a network of systems; not a tissue-specific disease state

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- **Multi-dimensional data sets will be the rule; we need new tools to analyze data that yield new insights**

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- **Drug and diagnostic development in an age of personalized medicine require a new business model**

Messages from the EC Scientific Retreat

- Cancer must be analyzed as a network of systems; not a tissue-specific disease state
- Multi-dimensional data sets will be the rule; we need new tools to analyze data that yield new insights
- Drug and diagnostic development in an age of personalized medicine require a new business model
- **Teamwork is critical, and barriers that impede teamwork need to be eliminated**

Messages from the EC Scientific Retreat

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Messages from the EC Scientific Retreat

- Resistance to change within the clinical and scientific cultures is impeding progress
- The field must embrace the complexity and heterogeneity of cancer
- Nanotechnology is driving revolutionary advances and will open new avenues of research
- **There is a critical need for better incentives for collaboration and tissue collection**

Challenges Ahead

- NCI's ability to form public-private partnerships, particularly around drug development

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Challenges Ahead

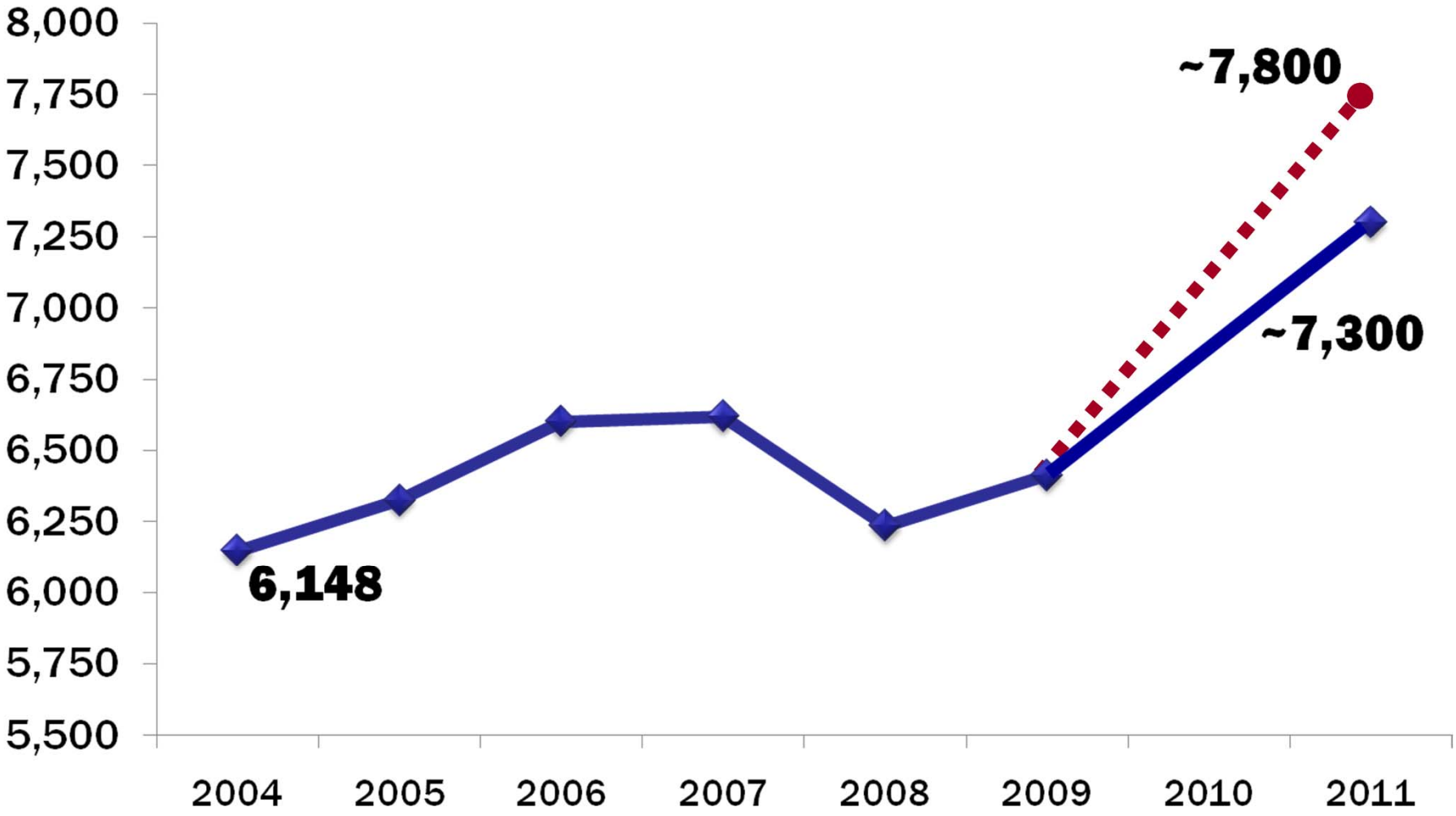
- NCI's ability to form public-private partnerships, particularly around drug development
- Reshaping clinical trials
- Increasing the base, to maintain momentum created by ARRA
- **Fostering innovative, collaborative scientific initiatives**


Patients & Families
www.cancer.gov

Preparing for the Fourth Quarter of FY 2010

- $317 million of ARRA funds still to be obligated, or about 25 percent
  - $164 million in grants
  - $148 million in contracts

Number of RPG Applications

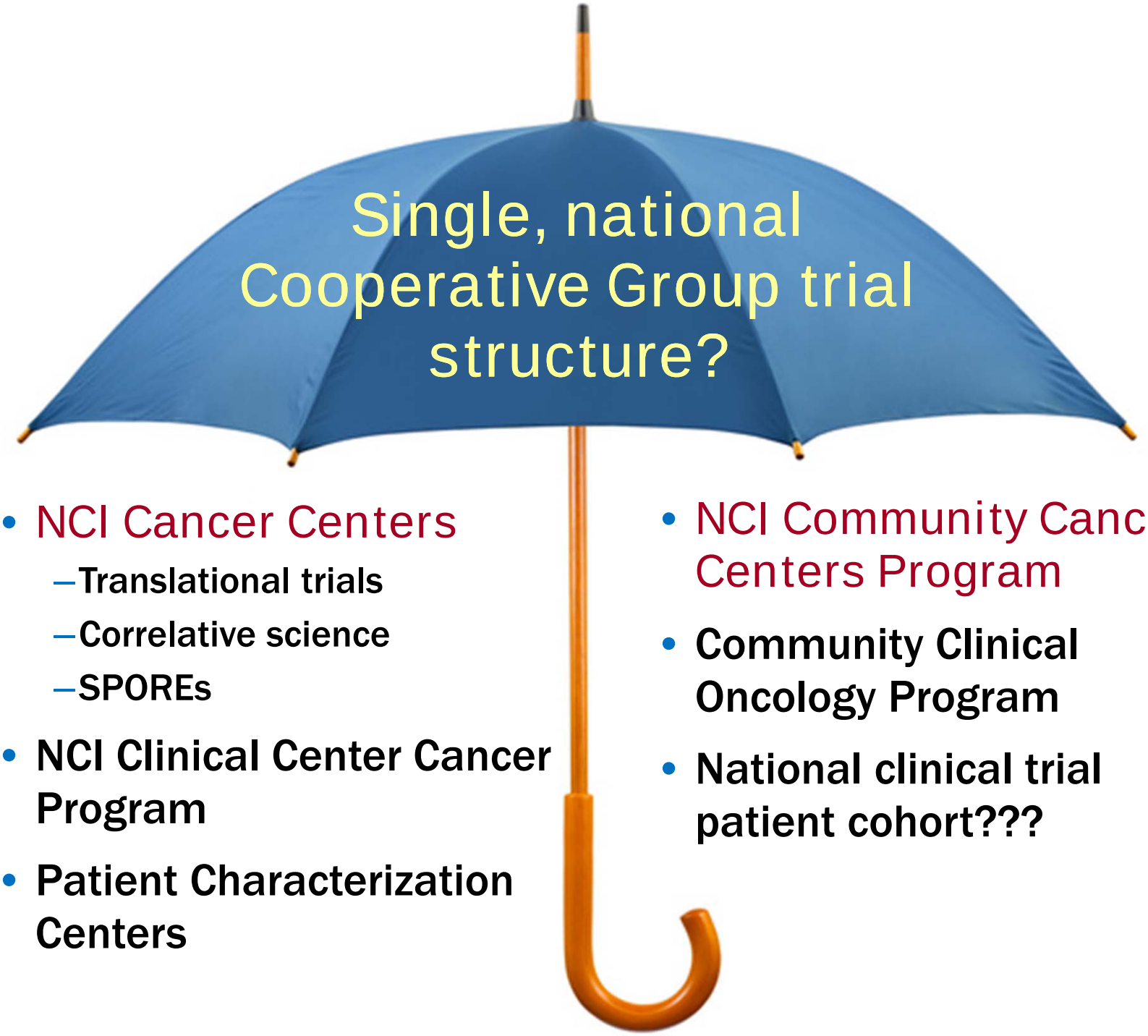


NCI's Investments

Despite below-inflation budgets, NCI has launched a number of important initiatives

- **Chemical Biology Consortium**
- **Functional Biology Consortium**
- **Physical Sciences-Oncology Centers**
- **Coordinating Center for Clinical Trials**
- **BIG Health Consortium**
- Target Discovery and Development Network
- **Advanced Technology Partnership Initiative**
- **Cancer Human Biobank (caHUB)**
- **NCI Community Cancer Centers Program**

If we ask ourselves…
"Where is the optimal integration of molecular cancer science and clinical research being conducted?"



- NCI Cancer Centers
  - Translational trials
  - Correlative science
  - SPOREs
- **NCI Clinical Center Cancer Program**
- **Patient Characterization Centers**
- NCI Community Cancer Centers Program
- **Community Clinical Oncology Program**
- **National clinical trial patient cohort???**