

NCI Director's Report

Norman E. Sharpless, M.D.

February 13, 2018

FY 2019 President's Budget

Source of Funding (dollars in millions)	FY17 Enacted	FY18 Annualized CR	FY19 President's Budget	FY19 President's Budget Addendum ¹
Appropriation	\$5,389	\$5,389	\$3,756	\$5,226
Rescission	-	-\$37	-	-
Secretary's Transfer for Unaccompanied Minors	-\$12	-	-	-
OAR HIV/AIDS Transfers	-\$17	-	-	-
Subtotal, adjusted budget authority	\$5,360	\$5,352	\$3,756	\$5,226
21 st Century Cures Act	\$300	\$300	\$400	\$400
Grand Total (Base & Cures)	\$5,660	\$5,652	\$4,156	\$5,626

¹Reflects NCI's portion of NIH's increase due to the Bipartisan Budget Act of 2018

Intergovernmental Affairs

Collaborating with FDA and CMS



Scott Gottlieb
Commissioner of FDA

- Oncology Center of Excellence
- Joint Training
- Data Sharing
- Compliance advice on cell manufacture



Seema Verma
Director, CMS

- Help with NGS coverage decision
- Data Sharing
- Discussions over enhanced coverage of clinical trials

Interactions with HHS

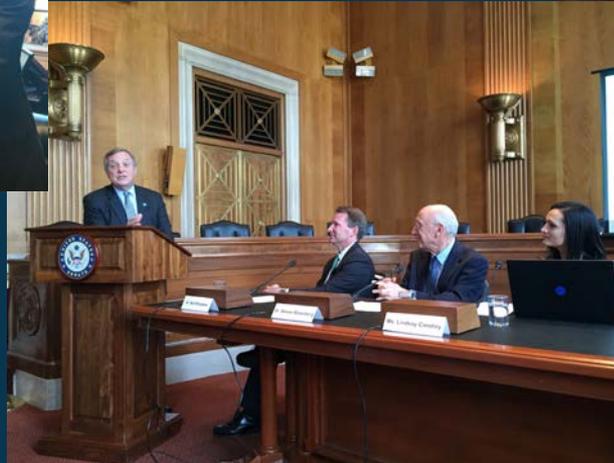


Alex M. Azar II
Secretary, HHS



Eric D. Hargan
Deputy Secretary, HHS

Congressional Outreach



President's Cancer Panel Report

March 2018

Promoting Value, Affordability, and Innovation in Cancer Drug Treatment



A Report to the President of the United States
from the President's Cancer Panel

Updates

Early Stage Investigators

MERIT

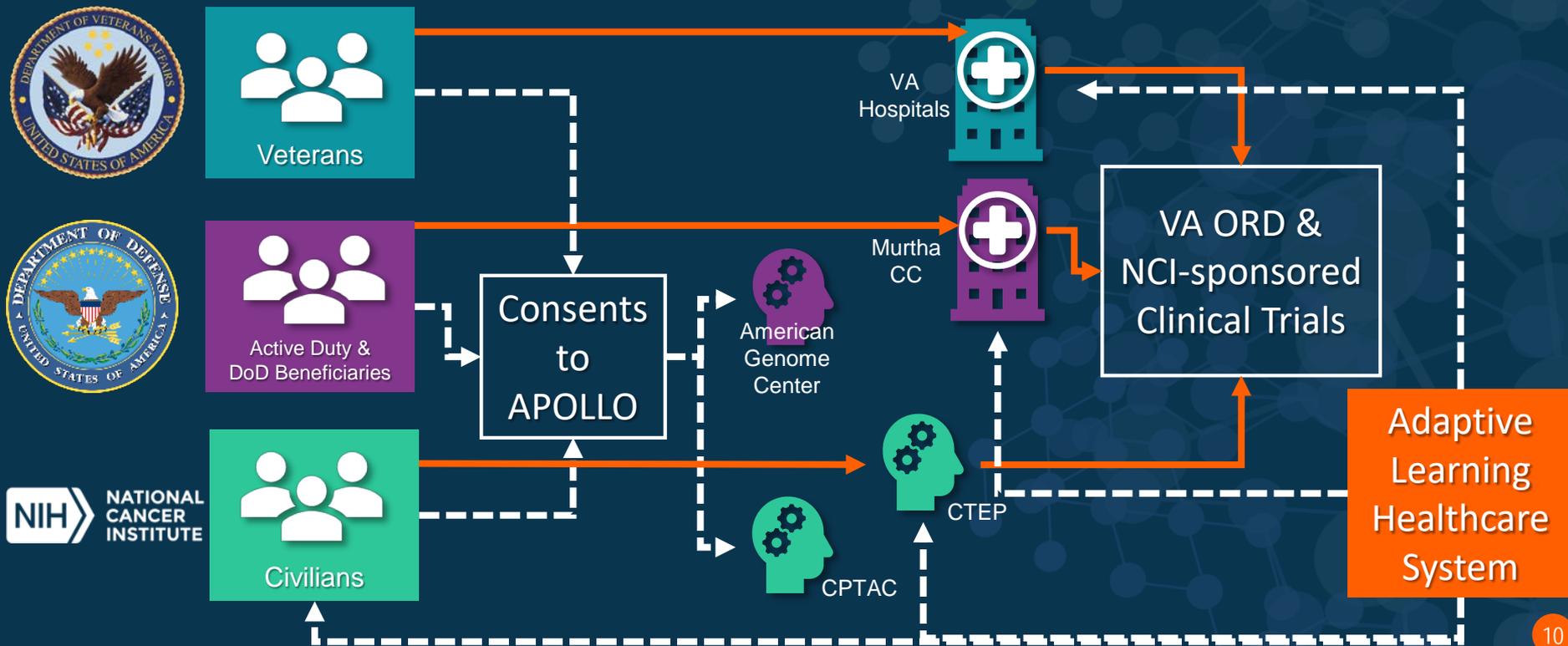
Method to Extend
Research in Time
R37 Award

- NCI recognizes that Early Stage Investigators (ESI) face challenges.
- In addition to increased ESI payline, NCI is announcing its new use of the MERIT Award in 2018.
- The award gives eligible investigators applying for first R01 the opportunity to obtain up to seven years of grant funding (5+2)
- This will provide critical time for ESIs to launch their careers and become more established before attempting renewal.

Applied Proteogenomics Organizational Learning and Outcomes (APOLLO)

Clinical Data

Research Data



Global Health Working Group



Global Health

- Deborah Bruner, RN, PhD
Emory University
- Satish Gopal, MD
UNC Chapel Hill

Sample questions

1. Balance of functions for CGH (representational vs. research)?
2. Portfolio analysis?
3. How to set priorities for NCI given the tremendous international burden of cancer?

SBIR / STTR Working Group



SBIR / STTR

- Elizabeth Jaffee, MD
Johns Hopkins University
- Mel Billingsley, PhD
Pennsylvania State
University

Sample questions

1. Are award sizes for the different phases of funding for SBIR/STTR appropriate?
2. How to improve review?
3. What resources in addition to funding should SBIR provide?
4. How to speed delivery of funds to small companies?

Informatics Working Group



Informatics

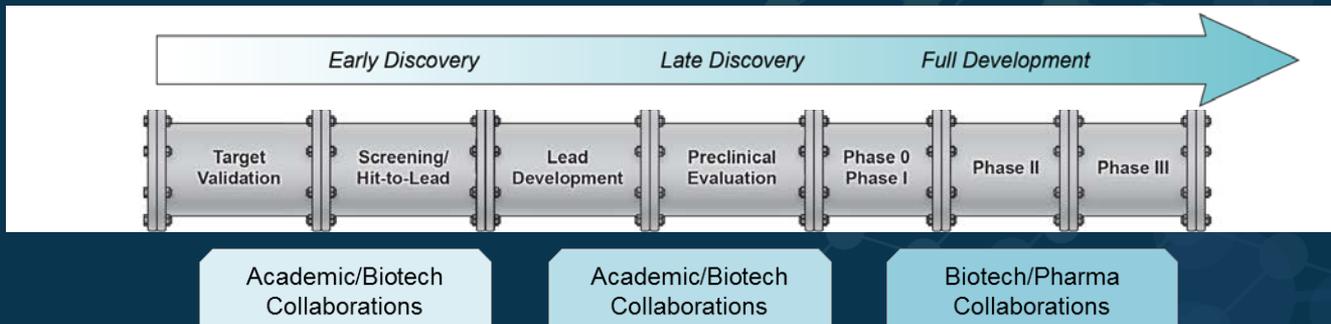
- Mia Levy, MD
Vanderbilt University
- Charles Sawyers, MD
Memorial Sloan Kettering
Cancer Center

- Provide input into the role of the CBIIT director, focusing particularly on whether the duties of a chief information officer should be separate
- Advise on expanding funding opportunities for data science and bioinformatics research across the NCI research portfolio and building a cancer-focused data science and bioinformatics workforce
- Provide guidance for improving data sharing to maximize the impact of cancer research on patients

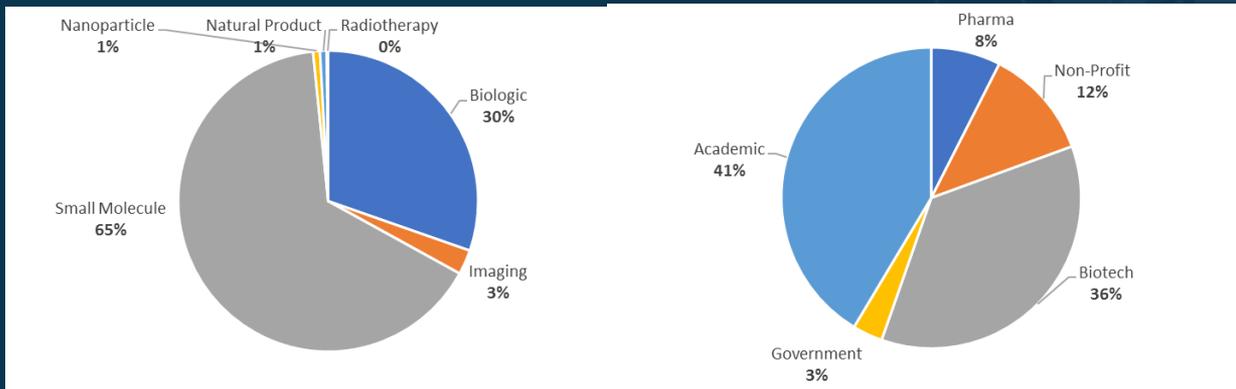
Cancer Moonshot Update

- Trans-NCI decision making process for FY18 & beyond
- Robust interest from community for all 10 recommendations
- New FY19 & reissued FY18 RFAs for NCAB approval at June & August meetings

NCI Experimental Therapeutics (NExT) Pipeline



*Projects enter the pipeline on a competitive basis at any stage of the pipeline
Since inception in 2009 NExT has received over 650 applications*



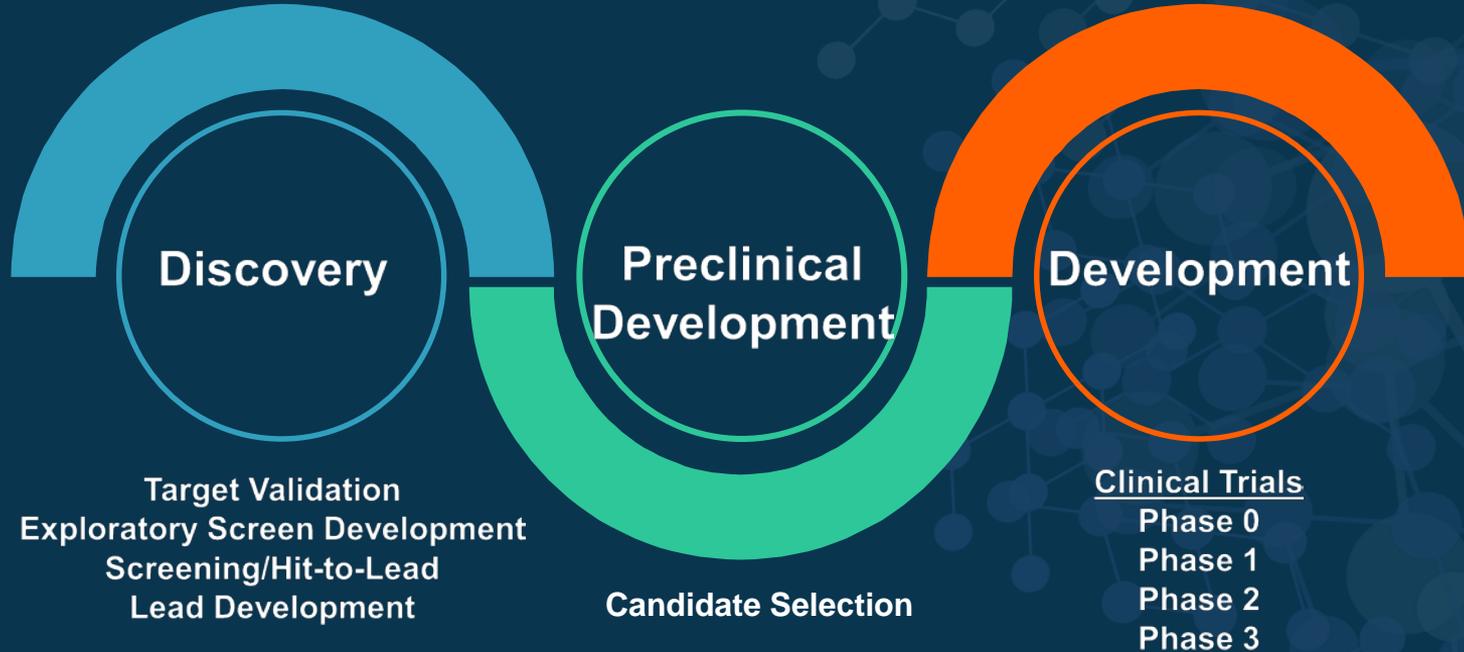
NEXt Pipeline

Artemis Endonuclease inhibitor
AAA ATPase p97 inhibitor
Taspase1 inhibitor
WDR5-MLL1 inhibitor
LDHA inhibitor
SHP2 inhibitor
PHGDH inhibitor

MCL1 Inhibitor
Mutant IDH1 inhibitor

DNMT1 Inhibitors (TdCyd)
11-1F4 mAb Amyloidosis

Endoxifen
Mer Kinase Inhibitors
NIR Fluorophore
EGFR Panitumumab
LUM015

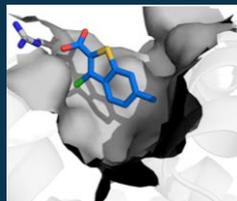


Mcl-1 Inhibitor Discovery by Fragment-Based Methods & Structure-Based Design

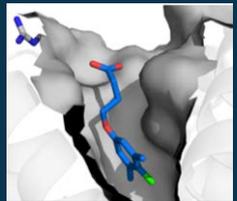
Hit to Lead

Lead Optimization

In vivo Optimization



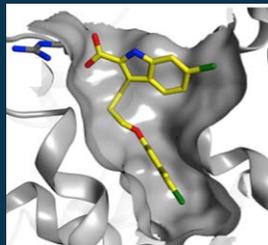
$K_i = 131 \mu\text{M}$



$K_i = 60 \mu\text{M}$

Fragment hits

Structure-guided
fragment merging



Mcl-1 $K_i = 55 \text{ nM}$

Binding interface
Expansion

Mcl-1 $K_i = 23 \text{ nM}$

Structure-guided
Tethering

Mcl-1 $K_i = 0.39 \text{ nM}$
H929 $GI_{50} = 1.2 \mu\text{M}$

Med. Chem.
Optimization

Mcl-1 $K_i = <0.3 \text{ nM}$
H929 $GI_{50} = <0.3 \mu\text{M}$

> 200,000x improvement in affinity for target

Likely candidate profile

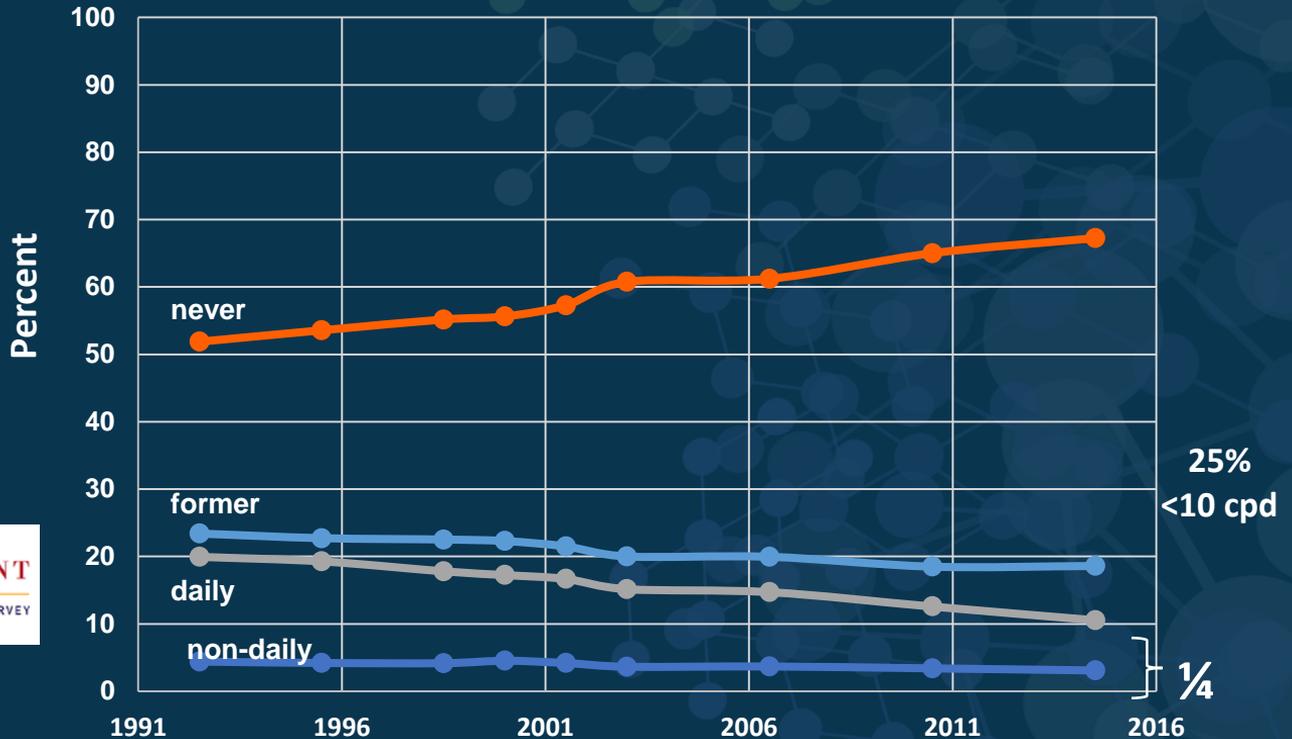
- ✓ $K_i < 0.3 \text{ nM}$ to Mcl-1
- ✓ Cellular $IC_{50} < 100 \text{ nM}$
- ✓ Oral bioavailability
- ✓ Robust pharmacodynamic response

Current work focused on identification of clinical candidate by profiling compounds for *in vivo* efficacy and therapeutic window.

Leads feature

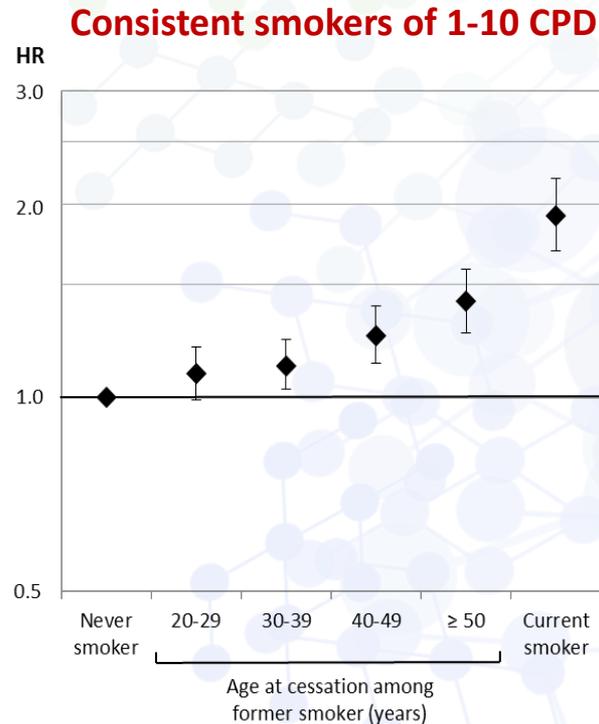
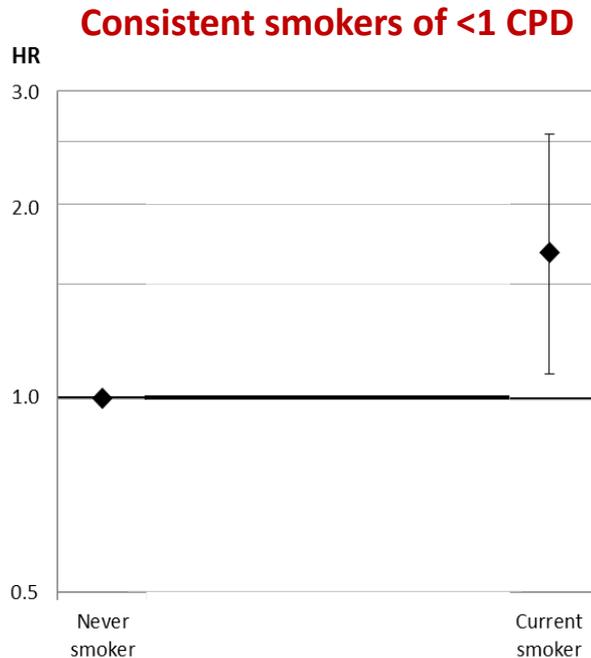
- $K_i < 0.3 \text{ nM}$ to Mcl-1
- $IC_{50} < 300 \text{ nM}$ in multiple cancer cell-lines
- Target-based on-mechanism activity (Caspase activation, JC-1/BH3 profiling, co-IP, multiplex PD apoptosis assays)
- Good PK properties

Cigarette use in the United States



TOBACCO USE SUPPLEMENT
CURRENT POPULATION SURVEY

Lifelong consistent low-intensity smokers had increased risk of mortality vs. never-smokers



Rural Cancer Control Update

BACKGROUND

- 14-19% of the US population lives in non-metropolitan (rural) counties
- Notable challenges, compared to urban areas:
- Higher poverty
- Lower educational attainment
- Higher proportion of elderly individuals
- Lower access to health services
- Higher rates of behavioral risk factors (tobacco use, obesity)

Rural Cancer Control Update Planning & Engagement Efforts

- Rural Cancer Control Workshop, Memphis, May 4-5, 2017
- HRSA/NCI/CDC Webinar, Aug 30, 2017
- Understanding Definitions of Rural/Rurality, Oct 27, 2017
- National Academy Workshop on Small Populations, Jan 18-19, 2018
- Rural Health Policy Institute, Feb 6-8, 2018
- National Rural Health Assoc. Annual Meeting, May 8-11, 2018

Save the Date

Accelerating Research in Rural Cancer Control Conference

Natcher Conference Center
National Institutes of Health
Bethesda, Maryland
May 30-31, 2018

Program Committee Chair: Robin Vanderpool, University of Kentucky
<https://cancercontrol.cancer.gov/research-emphasis/meetings/arcc-meeting.html>.

Vision – *In progress*

- ‘Listening Tour’ to conclude in March
- Clearly, there are 3 Bins:
 - Things We Have to Do
 - Things We Want to Do
 - Things We Are Already Doing (but need ongoing investment)

RPG Pool

NCI Unsolicited R01 Awards

	FY2013	FY2014	FY2015	FY2016	FY2017
Number of Applications	4003	3847	4550	4758	5263
Number of Awards	582	578	623	650	650
Success rate (%)	15%	15%	14%	14%	12%
Average cost (\$M)	0.392	0.413	0.443	0.451	0.460
Total amount (\$M)	228	239	276	293	299

NCI RPG Pool (without SBIR/STTR)

	FY2013	FY2014	FY2015	FY2016	FY2017
Competing (billion)	0.404	0.450	0.508	0.513	0.514
Non- competing (\$Bn)	1.450	1.407	1.419	1.454	1.534
Non- competing support (%)	94%	97%	100%	100%	100%
Total RPG (\$Bn)	1.854	1.858	1.927	1.967	2.070



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CANCER
INSTITUTE**

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