

An abstract graphic on the right side of the slide, consisting of a network of interconnected nodes and lines. The nodes are represented by circles of various sizes and colors, including shades of blue, green, and yellow. The lines connecting them are thin and light-colored, creating a complex, web-like structure that suggests a molecular or biological network.

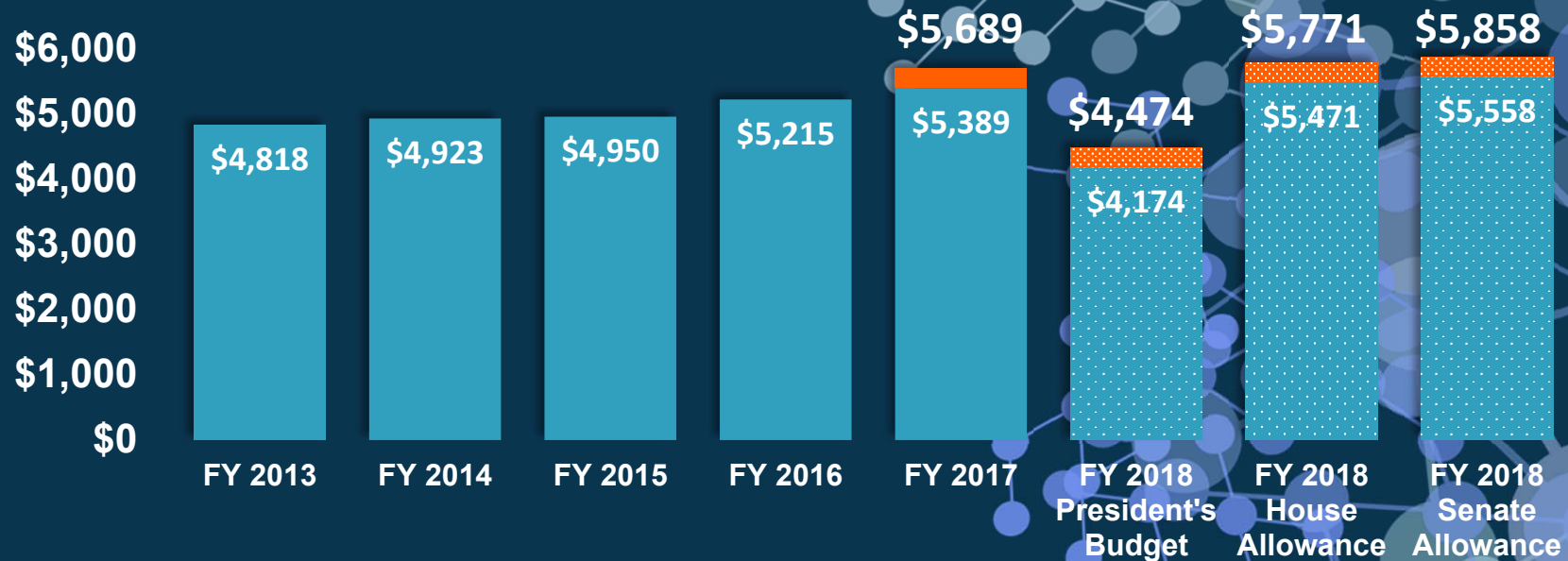
# NCI Director's Report

Norman E. Sharpless, M.D.

March 7, 2018

 NATIONAL CANCER INSTITUTE

# NCI Appropriations FY 2013-2018 (in millions)



# 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

---



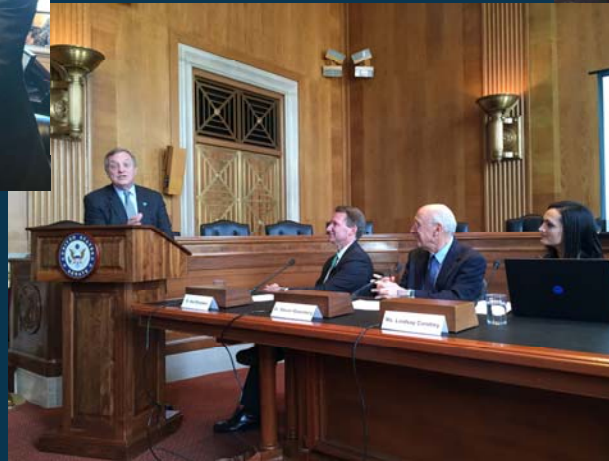
**Alex M. Azar II**  
Secretary, HHS



**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

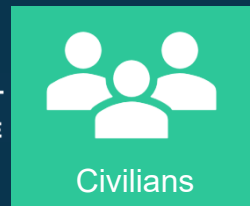
Research Data



Veterans



Active Duty & DoD Beneficiaries



Civilians

Consents to APOLLO

American Genome Center

CPTAC



VA Hospitals



Murtha CC



CTEP

VA ORD & NCI-sponsored Clinical Trials

Adaptive Learning Healthcare System

# 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

April 2017

Cancer Moonshot  
Implementation  
Teams Developed  
Scientific Proposals



May 2017



NCI Scientific  
Program Leaders  
reviewed and  
recommended

June 2017

BSA reviewed and  
recommended



Oct 2017



FY 2018 FOAs  
Released

# Partnership for Accelerating Cancer Therapies (PACT)

National Cancer Institute - Division of Cancer Treatment & Diagnosis

Cancer Immune Monitoring Analysis Centers (CIMACs)

Dana-Farber

Stanford

Mount Sinai

MD Anderson

AbbVie

Amgen

Boehringer  
Ingelheim

BMS

Celgene

Genentech

Gilead

GSK

Cancer Immunologic Data Commons (CIDC)

Dana-Farber  
Cancer  
Institute

Janssen

Novartis

Pfizer

Sanofi

# Two New Immunotherapy Networks

---

## ADULT CANCERS

Immuno-Oncology  
Translational  
Network

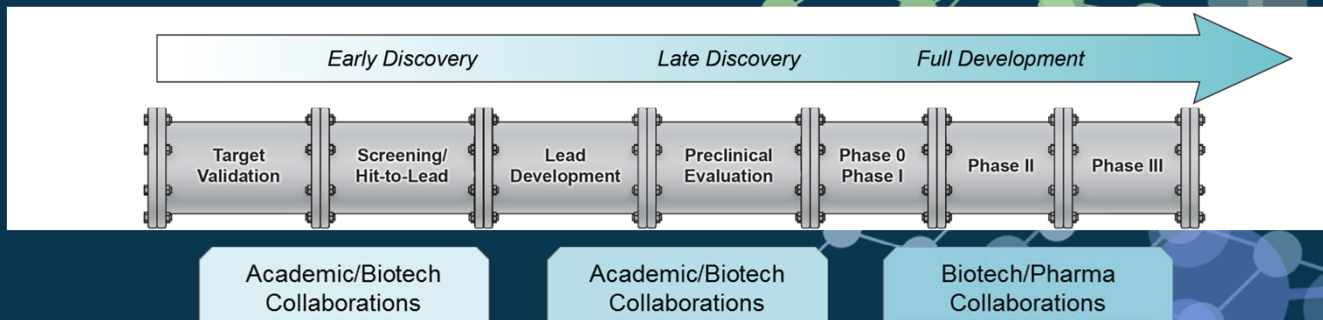
(IOTN, U01)

## PEDIATRIC CANCERS

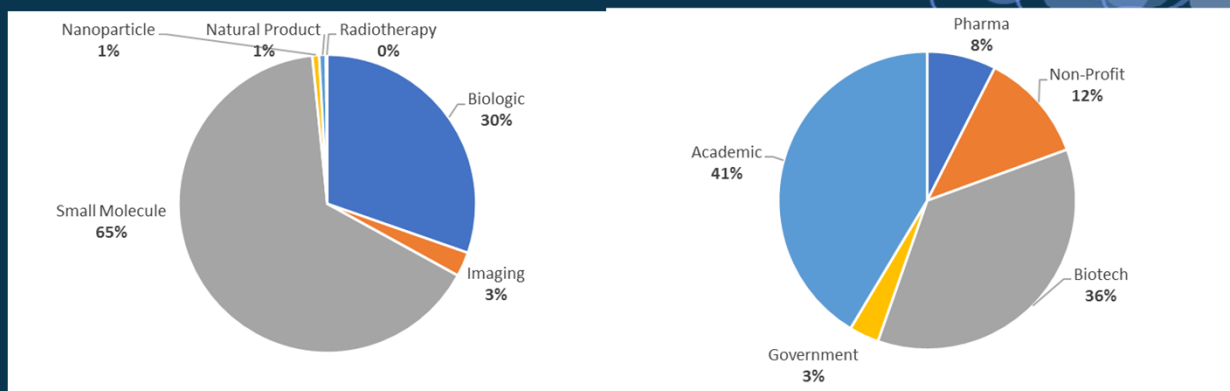
Pediatric  
Immunotherapy  
Discovery and  
Development  
Network

(PIDDN, U54)

# 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

Discovery

Preclinical  
Development

Development

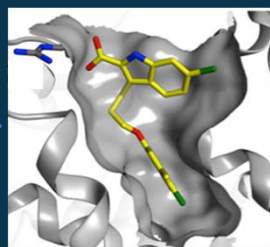
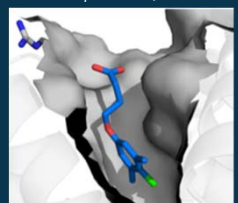
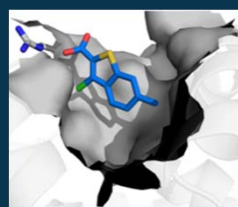
Target Validation  
Exploratory Screen Development  
Screening/Hit-to-Lead  
Lead Development

Candidate Selection

Clinical Trials  
Phase 0  
Phase 1  
Phase 2  
Phase 3



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



> 200,000x improvement in affinity for target

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

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

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

- 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.

**Fragment hits**

**Structure-guided fragment merging**

**Binding interface Expansion**

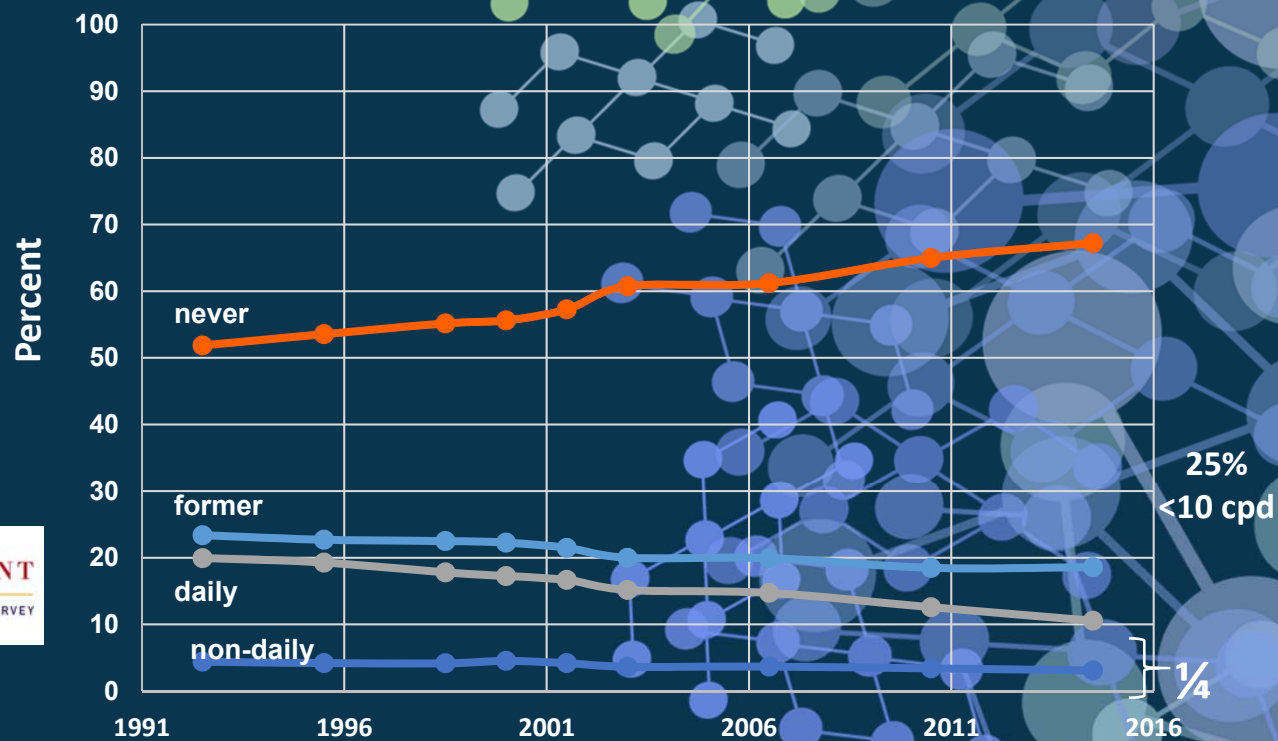
**Structure-guided Tethering**

**Med. Chem. Optimization**

**Leads feature**

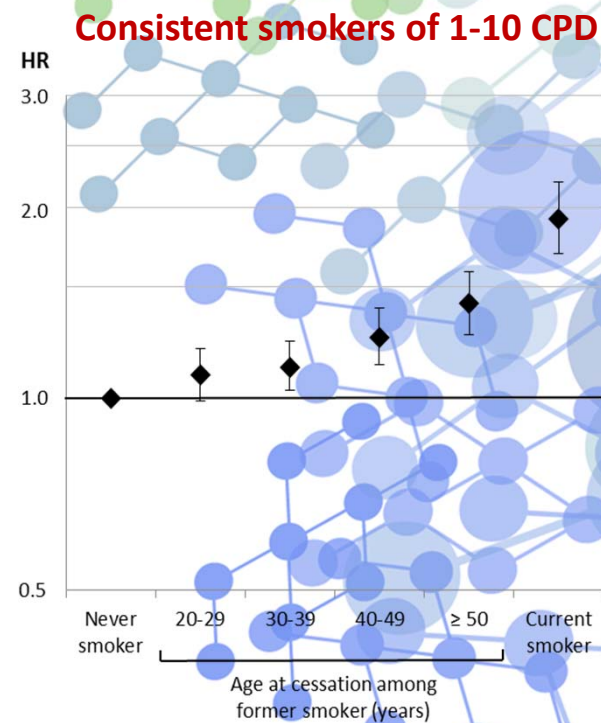
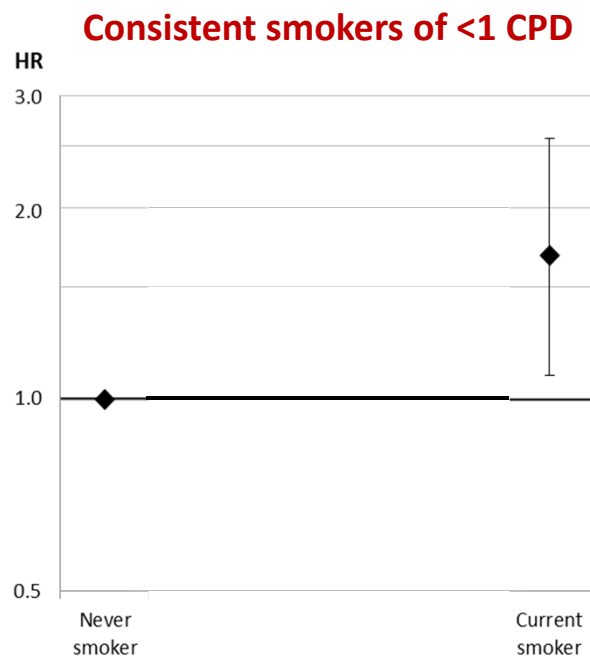
- $K_i < 0.3 \text{ nM}$  to Mcl-1
- $IC_{50} < 300 \text{ nM}$  in multiple cancer cell-lines
- Target-based on-mechanism activity (Caspase activation, JC-1/BH3 profiling, co-IP, multiplex PD apoptosis assays)
- Good PK properties

# 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

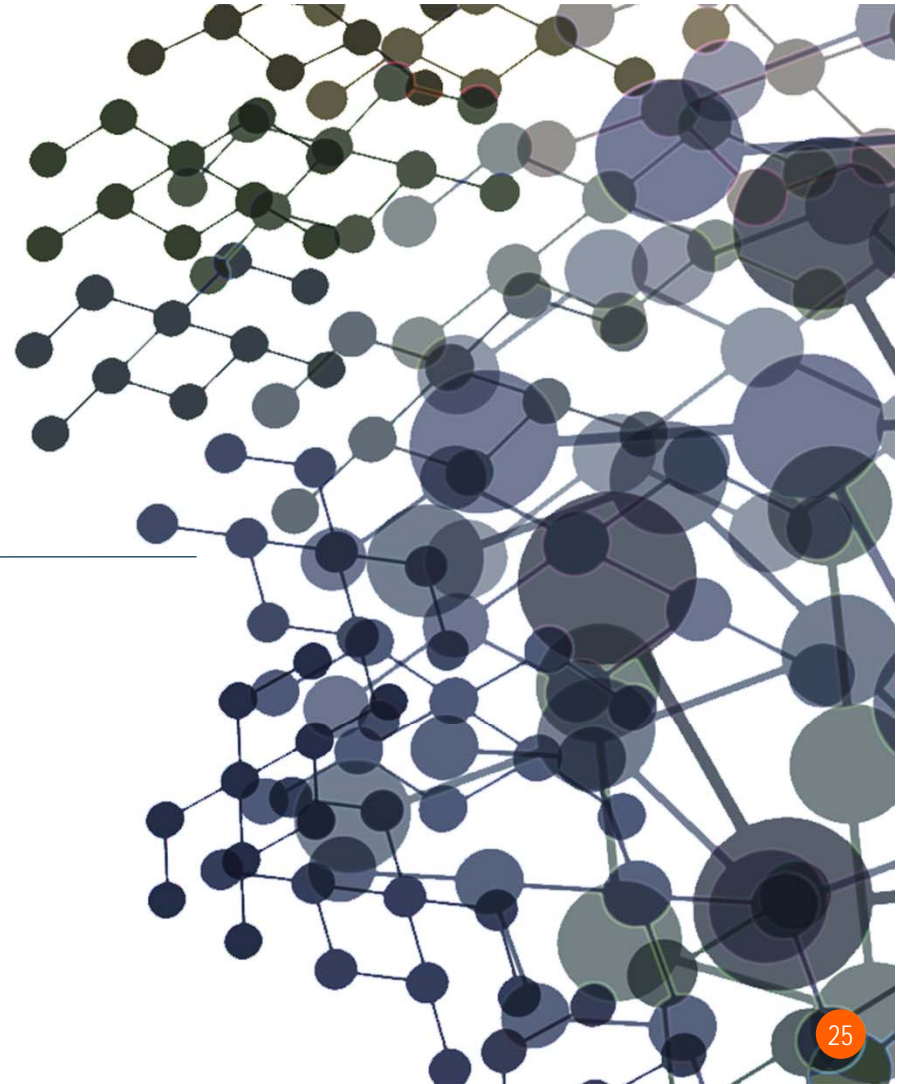
Natcher Conference Center  
National Institutes of Health  
Bethesda, Maryland  
May 30-31, 2018

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

# NCI-MATCH

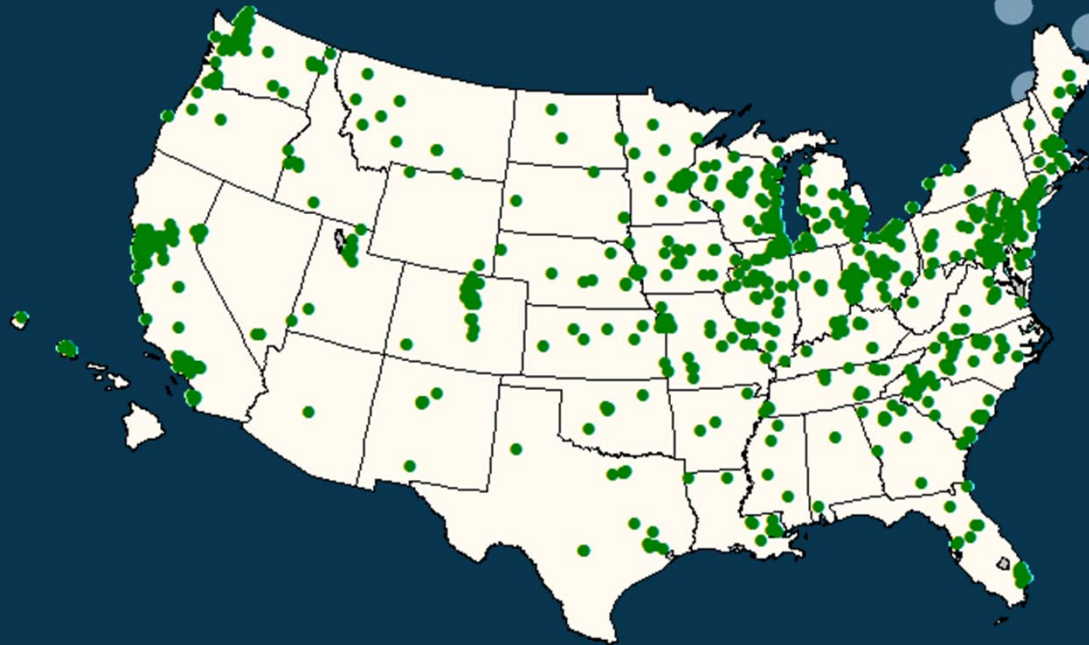
Molecular Analysis for Therapy Choice

 NATIONAL CANCER INSTITUTE



# NCI Molecular Analysis for Therapy Choice (NCI-MATCH)

---



- Precision medicine trial to explore treating patients based on the molecular profiles of their tumors
- **1,089** sites in U.S. across NCTN and NCORP

# NCI Molecular Analysis for Therapy Choice (NCI-MATCH)

---

## *Rare Variant Initiative:*

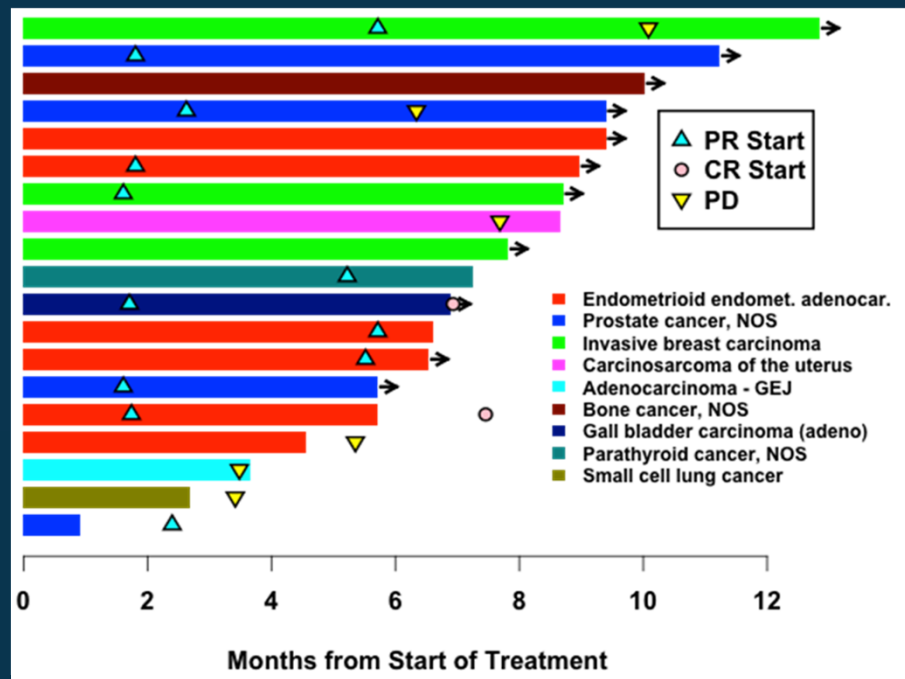
- Patients with low frequency mutations (< 2%) where well qualified drugs/targets available
- Foundation Medicine, Caris Life Sciences, MDACC, MSKCC will notify treating physician at any of the MATCH sites when results of their NGS panel would make patient eligible for a MATCH treatment arm
- Results verified centrally by NCI-MATCH OncoPrint® assay
- RFP from other NGS providers posted August 2017 and received January 2018 to broaden the base of patients available to enroll in precision oncology studies

# NCI Molecular Analysis for Therapy Choice (NCI-MATCH)

Time period	# enrolled	# first samples submitted	# first sample fail	# assay complete	# assigned to Rx	# enrolled on Rx
Total Pre Pause	794	739	116	645	54	27
Total Post Pause	5,603	5,223	425	4,912	937	660
Overall Total Screening Cohort	<b>6,396</b>	5,962	544	5,560	992	<b>689</b>
Total Outside Assay	<b>74</b>	36	2	68	59	<b>45</b>



# First NCI-MATCH Efficacy Data: Nivolumab in MSI high cancers



- Median cycles 3.5 (range 1-13+ cycles)
- Median time to first response was 2.1 months (includes unconfirmed PRs)
- 6-Month PFS was 49% (95% CI: 32-67%)
- Median duration of response has not been reached (4-8+ months; 7/8 still under treatment at time of data cutoff)
- 11 patients remain on therapy at time of data cutoff

# 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)



**NATIONAL  
CANCER  
INSTITUTE**

[www.cancer.gov](http://www.cancer.gov)

[www.cancer.gov/espanol](http://www.cancer.gov/espanol)