Cancer Moonshot Update

W. Kimryn Rathmell, M.D., Ph.D.
Director, National Cancer Institute

129th Meeting of the Advisory Committee to the Director (ACD), NIH

December 13, 2024

@NCIDirector
@TheNCI

NIH · NATIONAL CANCER INSTITUTE

Initial Cancer Moonshot

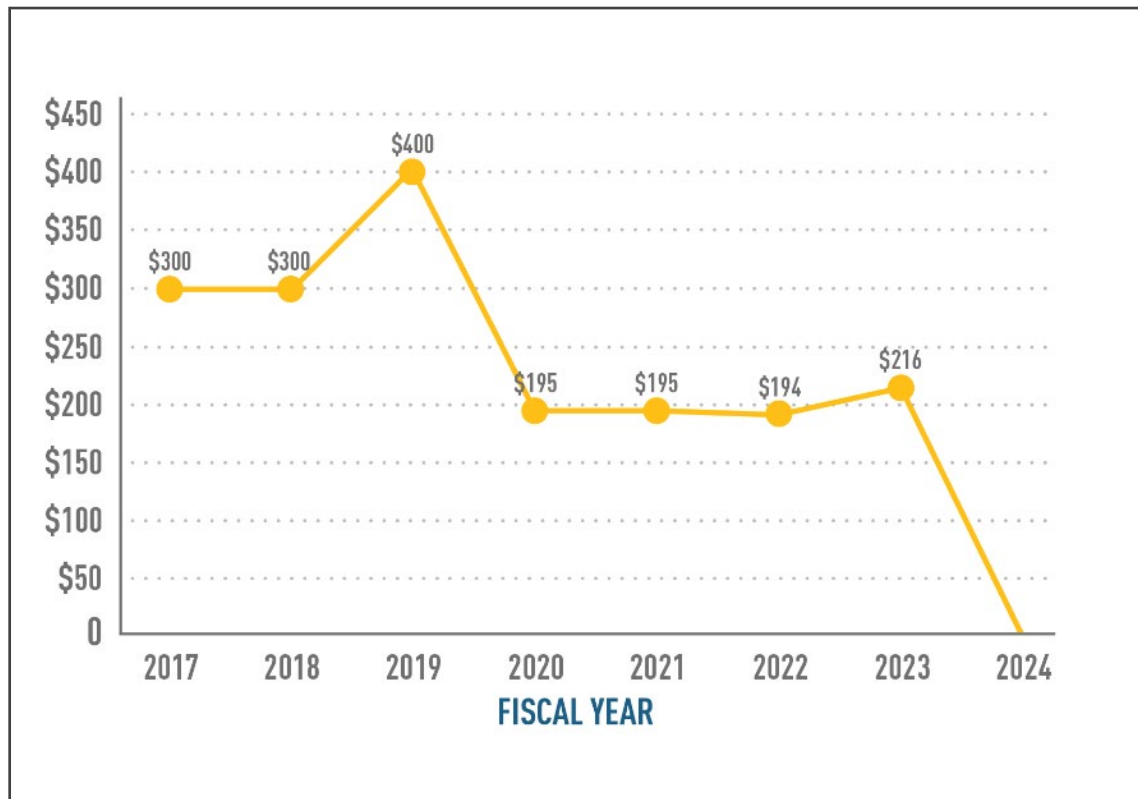## 3 BROAD GOALS

Generate New Knowledge

Enhance Collaboration

Improve Data Sharing

Blue Ribbon Panel Recommendations

1. Establish a network for direct patient engagement
2. Create a translational science network devoted exclusively to immunotherapy
3. Develop ways to overcome cancer's resistance to therapy
4. Build a National Cancer Data Ecosystem
5. Intensify research on the major drivers of childhood cancers
6. Minimize cancer treatment's debilitating side effects
7. Expand use of proven cancer prevention and early detection strategies
8. Mine past patient data to predict future patient outcomes
9. Develop a 3-D cancer atlas
10. Develop new cancer technologies

Cancer Moonshot Funding Authorized Under the 21st Century Cures Act
(dollars in millions)

Chart values by fiscal year:
- 2017: $300
- 2018: $300
- 2019: $400
- 2020: $195
- 2021: $195
- 2022: $194
- 2023: $216
- 2024: 0

FISCAL YEAR

Goals of the reignited Cancer Moonshot

- Reduce U.S. cancer mortality rate by 50% by 2047

- Improve the experience of people and their families living with and surviving cancer

"Reignited" Cancer Moonshot - 2022

First Cancer Cabinet Meeting, at the White House on March 16, 2022.

"[The Cancer Cabinet will] drive a **whole-of-government** effort to unleash every possibility within our power, within their jurisdictions."

—*President Joe Biden*

All of Government Approach: Cancer Cabinet

ARPA-H   CDC   CMS   DOC   NIH   USDA   NCI

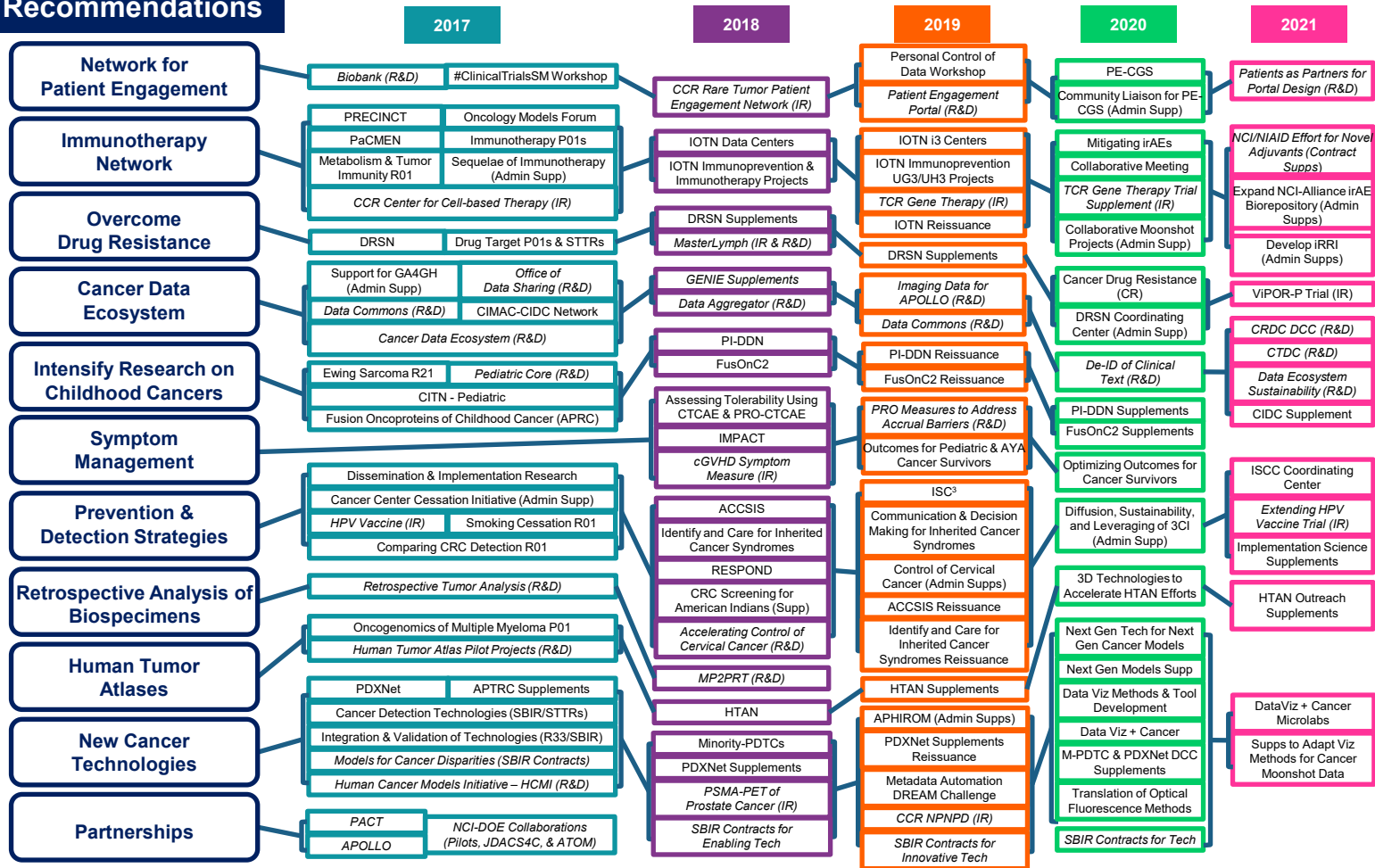HHS   DOL   NASA   DOD   DOE   EPA   FDA

VA

Delivering on the Blue Ribbon Panel Recommendations

CANCER MOONSHOT
BLUE RIBBON PANEL
REPORT 2016

Implementation of Recommendations

Blue Ribbon Panel Recommendations

Recommendation	2017	2018	2019	2020	2021
Network for Patient Engagement	Biobank (R&D); #ClinicalTrialsSM Workshop	CCR Rare Tumor Patient Engagement Network (IR)	Personal Control of Data Workshop; Patient Engagement Portal (R&D)	PE-CGS; Community Liaison for PE-CGS (Admin Supp)	Patients as Partners for Portal Design (R&D)
Immunotherapy Network	PRECINCT; Oncology Models Forum; PaCMEN; Immunotherapy P01s; Metabolism & Tumor Immunity R01; Sequelae of Immunotherapy (Admin Supp); CCR Center for Cell-based Therapy (IR)	IOTN Data Centers; IOTN Immunoprevention & Immunotherapy Projects	IOTN i3 Centers; IOTN Immunoprevention UG3/UH3 Projects; TCR Gene Therapy (IR); IOTN Reissuance	Mitigating irAEs; Collaborative Meeting; TCR Gene Therapy Trial Supplement (IR); Collaborative Moonshot Projects (Admin Supp)	NCI/NIAID Effort for Novel Adjuvants (Contract Supps); Expand NCI-Alliance irAE Biorepository (Admin Supps); Develop iRRI (Admin Supps)
Overcome Drug Resistance	DRSN; Drug Target P01s & STTRs	DRSN Supplements; MasterLymph (IR & R&D)	DRSN Supplements	Cancer Drug Resistance (CR); DRSN Coordinating Center (Admin Supp)	
Cancer Data Ecosystem	Support for GA4GH (Admin Supp); Office of Data Sharing (R&D); Data Commons (R&D); CIMAC-CIDC Network; Cancer Data Ecosystem (R&D)	GENIE Supplements; Data Aggregator (R&D)	Imaging Data for APOLLO (R&D); Data Commons (R&D)	De-ID of Clinical Text (R&D)	ViPOR-P Trial (IR); CRDC DCC (R&D); CTDC (R&D); Data Ecosystem Sustainability (R&D); CIDC Supplement
Intensify Research on Childhood Cancers	Ewing Sarcoma R21; Pediatric Core (R&D); CITN - Pediatric; Fusion Oncoproteins of Childhood Cancer (APRC)	PI-DDN; FusOnC2	PI-DDN Reissuance; FusOnC2 Reissuance	PI-DDN Supplements; FusOnC2 Supplements	
Symptom Management		Assessing Tolerability Using CTCAE & PRO-CTCAE; IMPACT; cGVHD Symptom Measure (IR)	PRO Measures to Address Accrual Barriers (R&D); Outcomes for Pediatric & AYA Cancer Survivors	Optimizing Outcomes for Cancer Survivors	
Prevention & Detection Strategies	Dissemination & Implementation Research; Cancer Center Cessation Initiative (Admin Supp); HPV Vaccine (IR); Smoking Cessation R01; Comparing CRC Detection R01	ACCSIS; Identify and Care for Inherited Cancer Syndromes; RESPOND; CRC Screening for American Indians (Supp); Accelerating Control of Cervical Cancer (R&D)	ISC³; Communication & Decision Making for Inherited Cancer Syndromes; Control of Cervical Cancer (Admin Supps); ACCSIS Reissuance; Identify and Care for Inherited Cancer Syndromes Reissuance	Diffusion, Sustainability, and Leveraging of 3CI (Admin Supp)	ISCC Coordinating Center; Extending HPV Vaccine Trial (IR); Implementation Science Supplements
Retrospective Analysis of Biospecimens	Retrospective Tumor Analysis (R&D)				
Human Tumor Atlases	Oncogenomics of Multiple Myeloma P01; Human Tumor Atlas Pilot Projects (R&D)	MP2PRT (R&D)	HTAN Supplements	3D Technologies to Accelerate HTAN Efforts	HTAN Outreach Supplements
New Cancer Technologies	PDXNet; APTRC Supplements; Cancer Detection Technologies (SBIR/STTRs); Integration & Validation of Technologies (R33/SBIR); Models for Cancer Disparities (SBIR Contracts); Human Cancer Models Initiative – HCMI (R&D)	HTAN; Minority-PDTCs; PDXNet Supplements; PSMA-PET of Prostate Cancer (IR); SBIR Contracts for Enabling Tech	APHIROM (Admin Supps); PDXNet Supplements Reissuance; Metadata Automation DREAM Challenge; CCR NPNPD (IR); SBIR Contracts for Innovative Tech	Next Gen Tech for Next Gen Cancer Models; Next Gen Models Supp; Data Viz Methods & Tool Development; Data Viz + Cancer; M-PDTC & PDXNet DCC Supplements; Translation of Optical Fluorescence Methods; SBIR Contracts for Tech	DataViz + Cancer Microlabs; Supps to Adapt Viz Methods for Cancer Moonshot Data
Partnerships	PACT; APOLLO; NCI-DOE Collaborations (Pilots, JDACS4C, & ATOM)				

Claire McCarthy, Ph.D., NCI Division of Cancer Biology

1. Establish a network for direct patient engagement

Participant Engagement and Cancer Genome Sequencing (PE-CGS) Network

Engaging Participants

Making Genomic Discoveries

Determining Best Practices for Engagement

1. Establish a network for direct patient engagement

The MyPART (My Pediatric and Adult Rare Tumor) Network

1. Establish a network for direct patient engagement

NCI-CONNECT Rare Brain and Spine Tumor Network

Building partnerships to help patients with rare brain and spine tumors

2. Create a translational science network devoted exclusively to immunotherapy

Immuno-Oncology Translational Network (IOTN)

NCI Center for Cell-Based Therapy (CCT)

Cancer Immune Monitoring and Analysis Centers (CIMACs) and the Cancer Immunologic Data Commons (CIDC)

Pancreatic Cancer Microenvironment Network (PaCMEN)

PRE-medical Cancer Immunotherapy Network Canine Trials (PRECINCT)

Remarkable advances in immunotherapy since 2017

85

Anti-PD-1/L1
Antibody
FDA Approvals
(9 drugs)

- Across **24** cancer types
- Including 1 tumor-agnostic immunotherapy drug for any solid tumor with mismatch repair deficiency (dMMR) that is microsatellite instability-high (MSI-H)
- **22** in Non-Small Cell Lung Cancer alone

39

Non-PD-1/L1
Immuno-Oncology
Agent FDA
Approvals

- Across **16** cancer types
- **13** in Non-Hodgkins Lymphoma
- **10** in Melanoma

Source: Cancer Research Institute, cancerresearch.org

Pediatric Immunotherapy Network

GOAL: to develop and advance novel translational immunotherapy approaches for children and adolescents with solid tumors (including brain cancers).

Enabling Immunotherapy for High-Risk Group 3 Medulloblastoma via Systems Immunology
Hongbo Chi, Jiyang Yu
St. Jude Children's Research Hospital

Attacking the Immunopeptidome of Ewing Sarcoma
Crystal Mackall, Sabine Heitzeneder
Stanford

Personalized Neuroblastoma Vaccines
John M. Maris, Stephen P. Schoenberger
Children's Hospital of Philadelphia

Targeting Tumor and T Cell DNA Methylomes to Improve CAR T Cell Therapies for Diffuse Midline Glioma
Stephen C. Mack, Giedre Krenciute, Timothy N. Phoenix
St. Jude Children's Research Hospital

Immunotherapeutic Targeting of Gangliosides in Ewing Sarcoma
Robbie G. Majzner, Kimberly Stegmaier
Dana-Farber Cancer Institute

Bispecific Antibody Therapeutics for Neuroblastoma and Diffuse Midline Glioma
James M. Olson, Vandana Kalia
Seattle Children's Hospital

Critical progress: CAR T-cell therapy for pediatric solid tumors

Intravenous and intracranial GD2-CAR T cells for H3K27M+ diffuse midline gliomas

Monje et al, *Nature*, 13 November 2024

- DIPG median survival: 11 months

- Only 10% of patients survive more than two years after diagnosis

- Therapy shrank children's brain tumors and restored neurologic function in several patients

CAR T-Cell Therapy

1 Remove blood from patient to get T cells

2 Make CAR T cells in the lab
Insert gene for CAR

CAR T cell

CAR protein

3 Grow millions of CAR T cells

4 Infuse CAR T cells into patient

5 CAR T cells bind to cancer cells and kill them

T cell

Cancer cell

Antigen
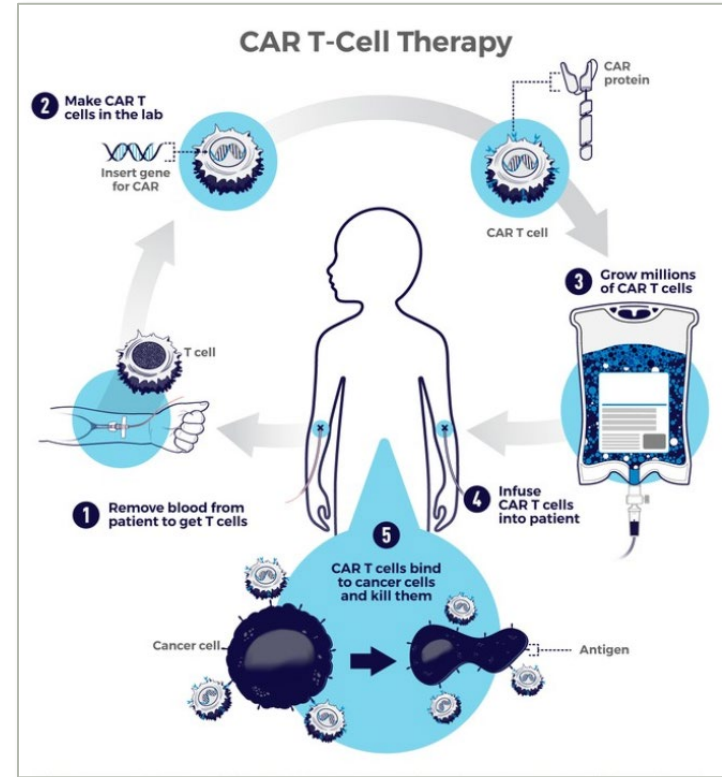
3. Develop ways to overcome cancer's resistance to therapy

- Combining Cancer Drugs
- Keeping Cancer Drugs inside Cells
- Erasing Reversible Modifications
- Altering the Tumor Microenvironment
- Simultaneously Testing Combinations
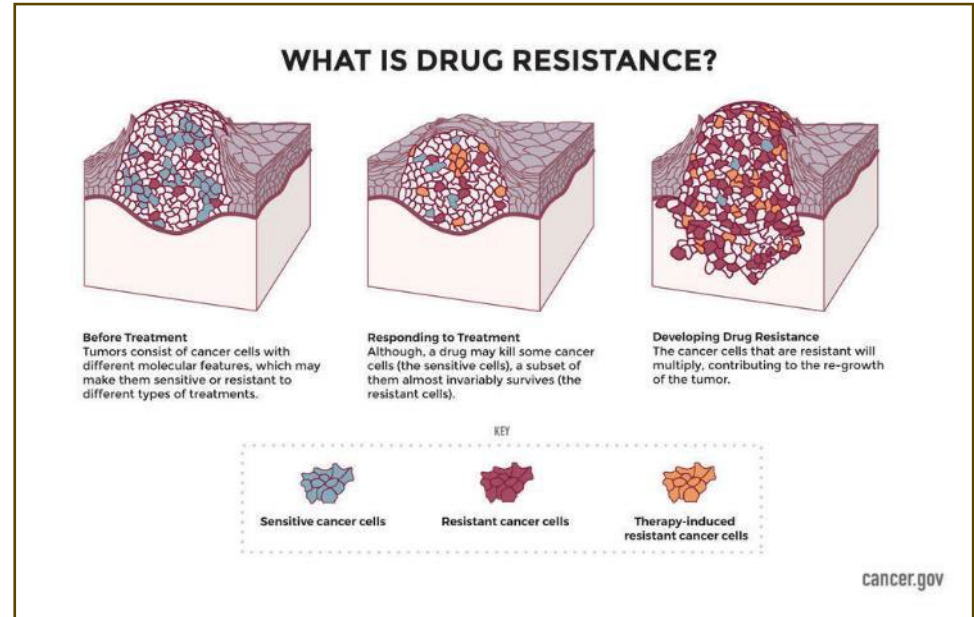
3. Develop ways to overcome cancer's resistance to therapy

NCI Formulary: A Public-Private Partnership

The NCI Formulary is comprised of

35 AGENTS

including monoclonal antibodies, inhibitors, and antagonists—with more coming soon.

These agents are provided by

12 COMPANIES[1]

with negotiations with other companies in process and planned.
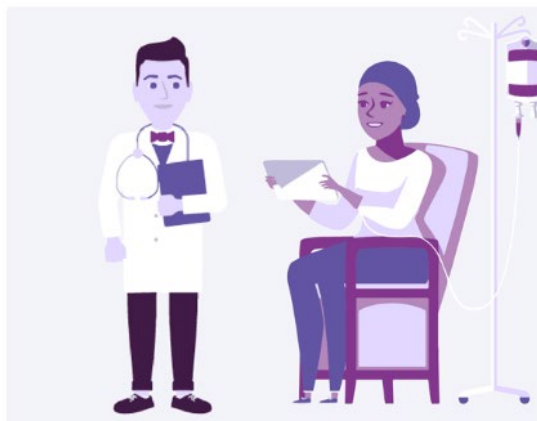
Investigators across

300+ NCI-AUDITED SITES[2]

can access these agents directly through the NCI.

Tackling drug resistance with a personalized "cocktail": The ViPOR Study

"Many of these patients who stopped responding to standard treatments would have otherwise died within a year, and now we have a good proportion who are still alive past two years, and some past four years. It's gratifying to see these long-term remissions and potential cures in patients."
- Christopher J. Melani, M.D., NCI

Read Justin's story in NCI's Annual Plan and Budget Proposal for FY 2025.

ClinicalTrials.gov: NCT03223610

4. Build a National Cancer Data Ecosystem

NCI CANCER RESEARCH DATA COMMONS (CRDC)

Data Commons + **Cloud Resources** + **Underlying infrastructure**

Learning from every pediatric patient with cancer

Developing optimal treatment based on large, comprehensive cancer research datasets

Improving health outcomes

NCI-funded projects that share their data via CRDC (examples)

- **APOLLO** - Applied Proteogenomics Organizational Learning and Outcomes Network
- **CCDI** - Childhood Cancer Data Initiative
- **CPTAC** - Clinical Proteomic Tumor Analysis Consortium
- **HTAN** - Human Tumor Atlas Network
- **TARGET** - Therapeutically Applicable Research to Generate Effective Treatments
- **TCGA** - The Cancer Genome Atlas

5. Intensify research on the major drivers of childhood cancers

| Fusion Oncoproteins in Childhood Cancers (FusOnC2) Consortium | → | Targeting Fusion Oncoproteins in Childhood Cancers (TFCC) Network |
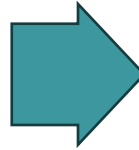
RESEARCH HIGHLIGHTS

Defined the molecular basis for the cancer-specific targeting properties of the fusion protein that drives synovial sarcoma *McBride et al, Nat Struct Mol Biol 2020.*	**Found that targeting TRIM8 can cause cancer cells to "overdose" on EWS/FLI and die** *Seong et al., Cancer Cell, 2022.*	**Identified a previously unknown role for FLI in transcriptional regulation in Ewing Sarcoma** *Boone et al., Oncogene, 2021.*

Childhood Cancer Data Initiative (CCDI)

+

Molecular Characterization Initiative (MCI)

Building a community centered around childhood cancer care and research data

cancer.gov/ccdi

Provides state-of-the-art molecular characterization to inform the best and most appropriate treatment

6. Minimize cancer treatment's debilitating side effects

National Standards for Cancer Survivorship Care

- Recommendations for health systems to apply to the survivors they serve.

- Defined standards for

  - essential health system policy and process components of survivorship care programs;

  - evaluation of the quality of survivorship care.

https://cancercontrol.cancer.gov/ocs/special-focus-areas/national-standards-cancer-survivorship-care

6. Minimize cancer treatment's debilitating side effects

Cancer Treatment Tolerability Consortium

AIMS OF THE U01 TOLERABILITY CONSORTIUM

ANALYSIS OF PRO-CTCAE AND CTCAE & OTHER PROS

- APPROACHES TO MISSING DATA
- GRAPHICAL REPRESENTATION
- PREDICTIVE MODELING
- PHARMACOKINETIC DATA
- ANALYSIS OF BASELINE SYMPTOMS, HOST FACTORS
- SUMMARY AND SCORING MEASURES
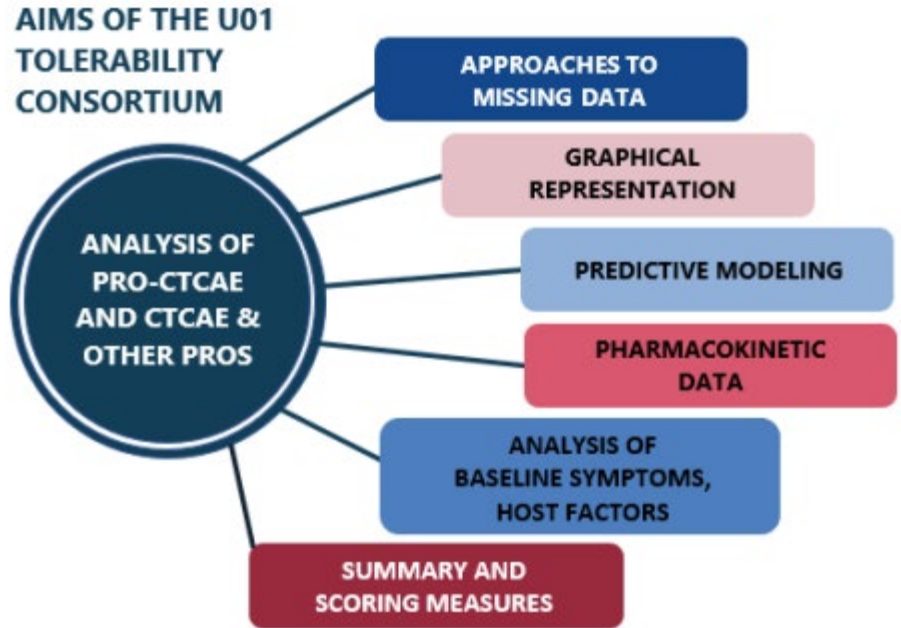
6. Minimize cancer treatment's debilitating side effects

Improving the Management of symPtoms during And following Cancer Treatment (IMPACT) consortium

Implementation and Evaluation of an Expanded Bilingual Electronic Symptom Management Program across a Multi-site, Fully-integrated Comprehensive Cancer Center

Enhanced, EHR-facilitated Cancer Symptom Control (E2C2) Pragmatic Clinical Trial

SIMPRO Research Center: Integration and Implementation of PROs for Symptom Management in Oncology Practice

7. Expand use of proven cancer prevention and early detection strategies

Primary Prevention of Cervical Cancer through Human Papillomavirus (HPV) Vaccination: The HPV Vaccine Trials

Accelerating Colorectal Cancer Screening and follow-up through Implementation Science (ACCSIS)

NCI modeling study estimates prevention and screening efforts averted 4.7M deaths from 5 cancer types

Self-Collection for HPV Testing to Prevent Cervical Cancer

Cancer Center Cessation Initiative

Announcement of "SHIP" trial network on self-sampling for cervical cancer prevention at White House (Jan. 25, 2024)

Readout of White House Cervical Cancer Forum

JANUARY 31, 2024

Last week, the Biden Cancer Moonshot hosted the White House Cervical Cancer Forum ↗ to recognize Cervical Cancer Awareness Month and spur action on education, prevention, early detection, and treatment.

As part of the Forum, National Cancer Institute (NCI) Director Kimryn Rathmell announced a new NCI-supported trial to drive progress on cervical cancer prevention. The brand new 'Last Mile' Initiative, Self-collection for HPV testing to Improve Cervical Cancer Prevention (SHIP) Trial Network ↗ aims to test the performance of

As part of the Forum, National Cancer Institute (NCI) Director Kimryn Rathmell announced a new NCI-supported trial to drive progress on cervical cancer prevention. The brand new 'Last Mile' Initiative, Self-collection for HPV testing to Improve Cervical Cancer Prevention (SHIP) Trial Network ↗ aims to test the performance of multiple self-collection devices for HPV, the leading driver of cervical cancer, so that cervical cancer screening can be brought closer to the people in the communities that are behind on screening.

White House Cervical Cancer Forum (Jan. 25, 2024)

Self-collection for HPV testing to Improve Cervical Cancer Prevention (SHIP) Trial Network

- SHIP trial network is a great example of:
  - ✓ Broad collaboration – within research and beyond, including federal and private sector partners
  - ✓ Addressing disparities
  - ✓ Engaging with the community, beneficiaries of research

8. Mine past patient data to predict future patient outcomes

Molecular Profiling to Predict Response to Treatment (MP2PRT) Program

Designed to:

- Perform next-generation sequencing on archived tumor and normal biospecimens collected from patients enrolled on completed clinical trials

- Analyze the molecular characterization and clinical data following hypotheses developed by teams of clinicians and scientists

NCI National Clinical Trials Network

NCI Community Oncology Research Program

ℹ Resulting data are available through the NCI Genomic Data Commons.

9. Develop a 3-D cancer atlas

Human Tumor Atlas Network

HTAN is a National Cancer Institute (NCI)-funded Cancer Moonshot[SM] initiative to construct 3-dimensional atlases of the dynamic cellular, morphological, and molecular features of human cancers as they evolve from precancerous lesions to advanced disease. (*Cell April 2020*)

Explore latest Data   Learn more about HTAN

Data Release V6 .1 (Last updated 2024-11-22)

14	21	2147	9286
Atlases	Organs	Cases	Biospecimens

data.humantumoratlas.org

NCI Human Tumor Atlas Network (HTAN)

15 papers across **5** *Nature* journals

Published Oct 30

nature portfolio

The Human Tumor Atlas Network (HTAN): exploring tumor evolution in time and space

January 14, 2025

Li Ding
Washington University

Shannon Hughes
National Cancer Institute

Ken Lau
Vanderbilt University

10. Develop new cancer technologies

Chimeric antigen receptor (CAR) T-cell therapy	Tumor-infiltrating lymphocyte (TIL)	CRISPR based gene editing	Pro-TAC
Antibody-drug conjugates (ADC)	microRNA, siRNA	Bacterial vectors	PDXNet
	Alpha-fold to enhance targeted therapy development	NCI Program for Natural Product Discovery	

Cancer Moonshot Scholars program – All of government, All of US talent

OCTOBER 29, 2024

Biden Cancer Moonshot Announces New Cohort of Cancer Moonshot Scholars and Awards $6 Million to the Next Generation of Innovators in Cancer Prevention, Treatment, and Diagnosis

The Cancer Moonshot Scholars program seeks to:

✓ **Advance cancer science**

✓ **Broaden the talent in the NCI R01 portfolio** by enhancing the number of applications from early-stage investigators from diverse backgrounds

✓ **Increase diversity of thought and approach** to cancer research

Cancer Moonshot Scholars

Kandy Velazquez, PhD
University of South Carolina
at Columbia

The Role of TGFβ2 and
Macrophages in Cancer
Cachexia

**Ramon Francisco
Barajas, MD**
Oregon Health & Science
University

Leveraging Biologically Specific PET/MRI
Monitoring and Therapeutic Modulation of
the Hypoxic Glioblastoma Tumor Immune
Microenvironment into Improved
Outcomes

**Chelsey Schlechter,
PhD, MPH**
Huntsman Cancer Institute
at the University of Utah

Partnerships to Reduce
Obesity in Community
Health Center Patients

Assessing Impact

Measuring Cancer Moonshot Outputs 2017 - 2023

>3,400
publications

89
clinical trials

78
patent filings

How the Cancer Moonshot Enhanced Collaboration
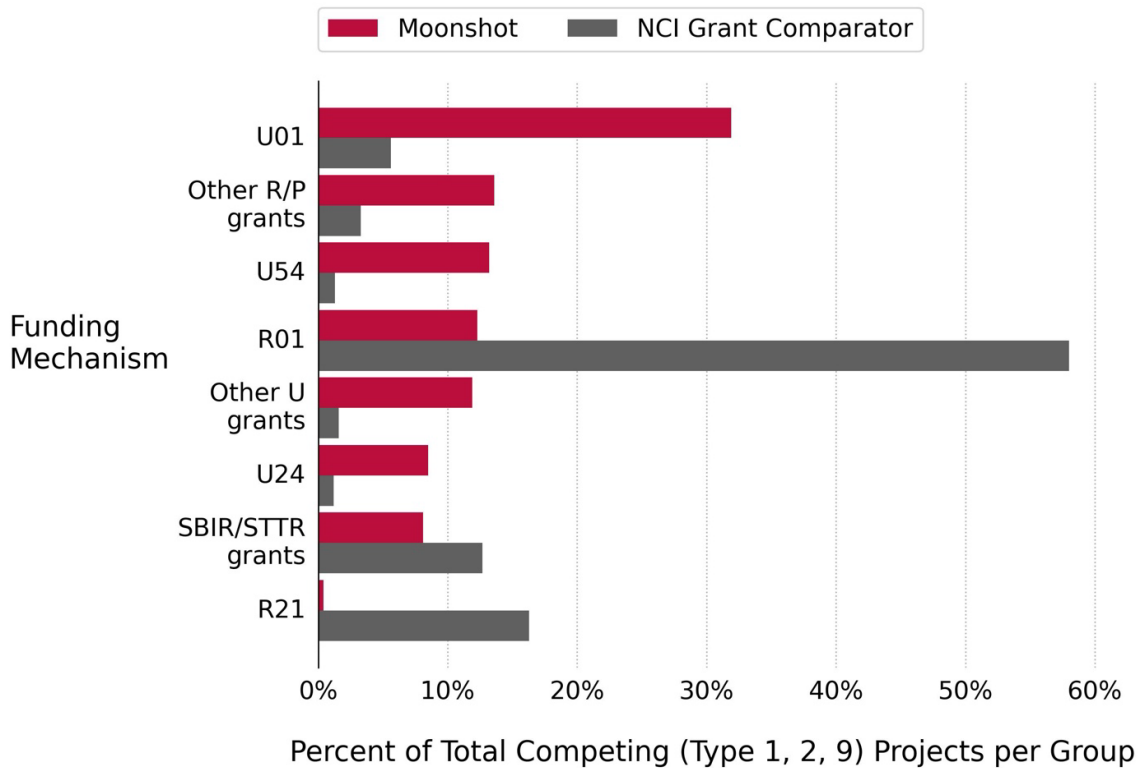
235 Cancer Moonshot grants

Cancer Moonshot Funding Supported New Collaborations and Sustained Ongoing Collaborations

4,168 Collaborations between Moonshot Extramural PIs after PIs received Moonshot funding

New collaborations (3,025)

Ongoing collaborations (1,143)

56% of new collaborations are directly Moonshot supported

Moonshot supported new collaborations (1,708)

No direct Moonshot support (1,317)

Moonshot supported ongoing collaborations (507)

No direct Moonshot support (636)

507 ongoing collaborations persisted with Moonshot support

Time range included: FY 2012 - FY 2023

30% of Cancer Moonshot Extramural PIs were New Investigators

Established Investigators (n=285)　　　New Investigators (n=131)

EIs with no prior NCI funding (n=42)

Early Stage Investigators (n=41)
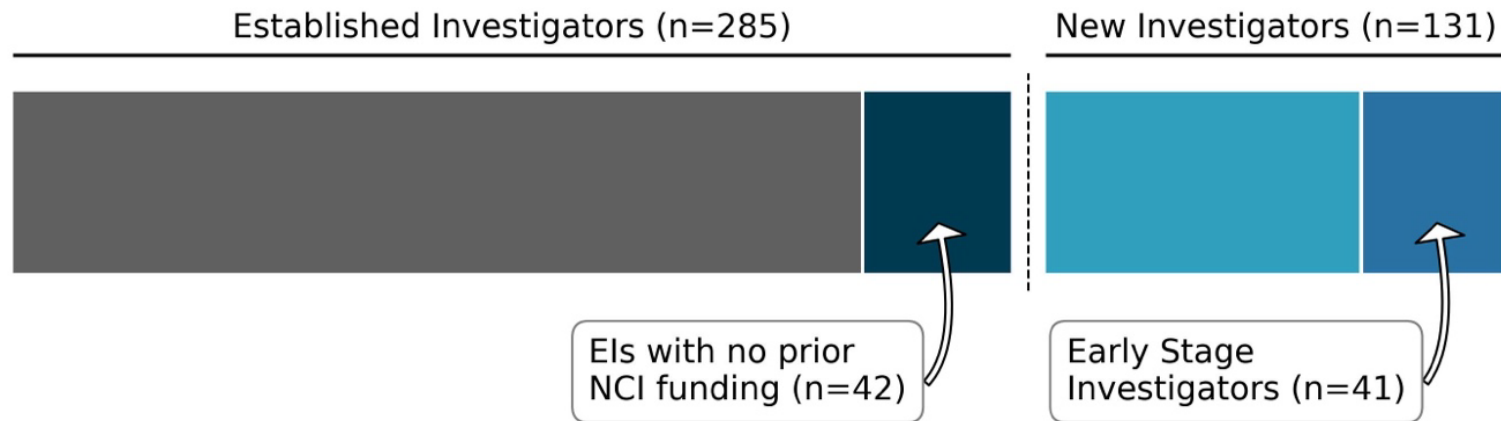
- 486 unique individuals have served as a PI (or MPI) on a Moonshot research grant, research grant subproject, or intramural project.

Methodology: Extramural PIs includes PI/MPIs of moonshot extramural awards (excluding supplements). Established, New, and Early Stage Investigator are based on NIH definitions.

Moonshot PIs Publishing in Nature Portfolio Journals Increased the Frequency of Sharing All Data

% of Moonshot manuscripts from Nature Portfolio journals
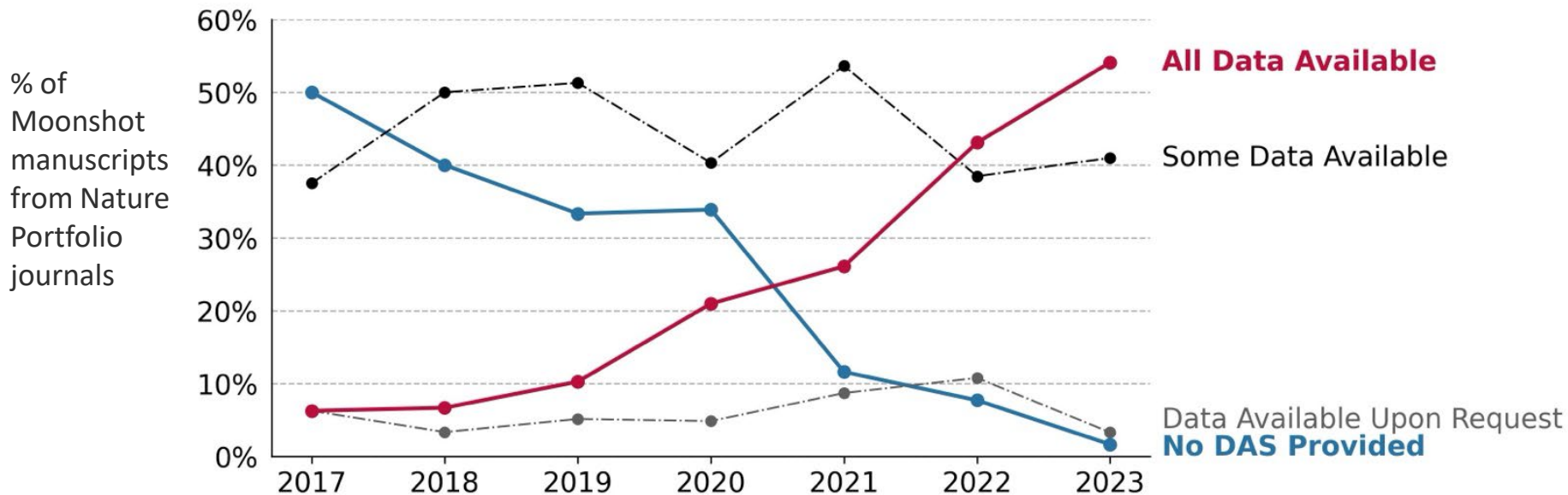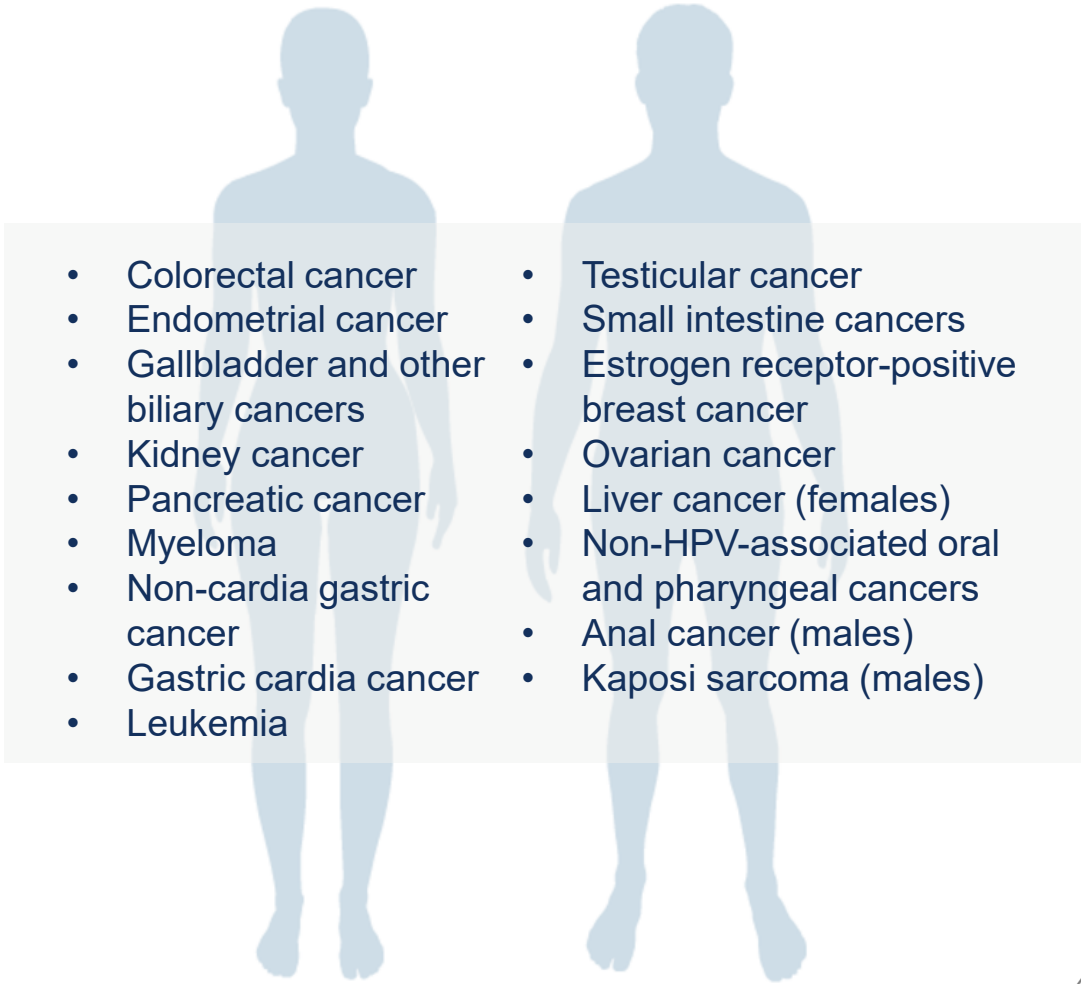
- This trend may be a reflection of data sharing behavior in the cancer research community due in part to ongoing cultural and policy shifts from the NIH, various major publishing groups, and others

Building on the Momentum of the Cancer Moonshot

NATIONAL CANCER INSTITUTE

Embracing new approaches to meet new challenges

Early-Onset Cancer Initiative

- Colorectal cancer
- Endometrial cancer
- Gallbladder and other biliary cancers
- Kidney cancer
- Pancreatic cancer
- Myeloma
- Non-cardia gastric cancer
- Gastric cardia cancer
- Leukemia

- Testicular cancer
- Small intestine cancers
- Estrogen receptor-positive breast cancer
- Ovarian cancer
- Liver cancer (females)
- Non-HPV-associated oral and pharyngeal cancers
- Anal cancer (males)
- Kaposi sarcoma (males)

Cancer Moonshot: Modernizing clinical studies

MyeloMATCH

Precision medicine trial testing new treatment combinations for AML and MDS, launched October 2024

Aims to enroll several thousand people within the first few years (new substudies rolled out over time)
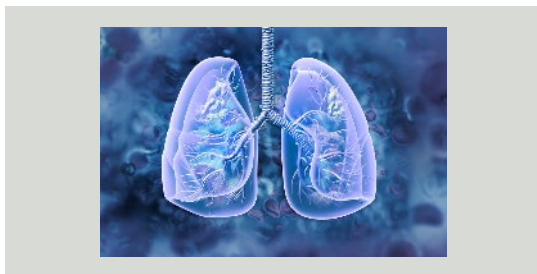
Pragmatica-Lung

Streamlined model, **removes many barriers** to access to clinical studies, launched April 2023

Testing if targeted therapy + immunotherapy for advanced NSCLC helps patients live longer vs. standard chemotherapy
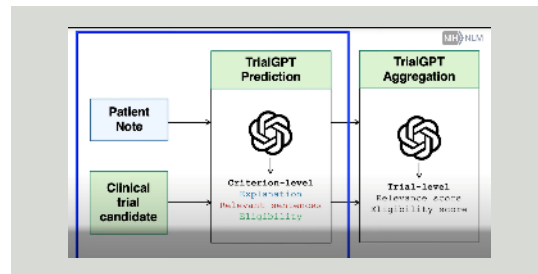
TrialGPT

AI algorithm to help speed up process of matching potential volunteers to clinical trials

Led by National Library of Medicine and NCI researchers

Nat Commun (Nov. 18, 2024)

Clinical Trials Innovation Unit (CTIU)
Piloting Innovations in Cancer Clinical Trials

- **Novel designs** - relaxed eligibility criteria, novel endpoints, pragmatic approaches
- **New technologies or biomarkers**
- **Strategies that allow for more effective care**
- **New data collection methodologies**

Partnering with FDA and extramural investigators

Crafting new approaches to bring more leading-edge clinical research to community settings

NCI Board of Scientific Advisors Ad Hoc Working Group in Support of Efforts to Enhance Community Cancer Research and Quality Care

William Dahut
ACS

Raymond Osarogiagbon
Vanderbilt

Suanna Steeby Bruinooge
ASCO
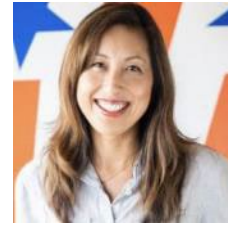
Anjee Davis
Fight Colorectal Cancer

Loretta Christensen
Indian Health Service

Augusto Ochoa
Louisiana State

Cornelia Ulrich
Huntsman Cancer Institute

Sanya Springfield
NCI

+20 members drawn from

- Federal agencies
- Nonprofits & advocacy orgs
- NCI-Designated Cancer Centers
- Research universities
- Others

Report presented 12/3/24

43

Eras of biomedical research

Traditional Era

Current Era

Next Era 360°

NIH NATIONAL CANCER INSTITUTE

NCI innovation is "360⁰"