# Deputy Director's Update

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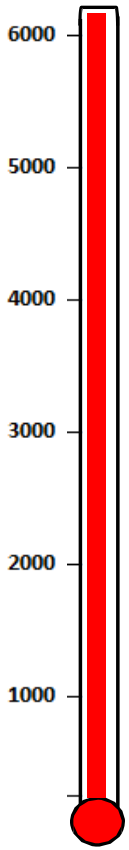
NIH NATIONAL CANCER INSTITUTE

**CTAC Meeting**
**July 12, 2017**

# Topics for Discussion

- NCI MATCH Trial
- NCI Patient-Derived Models Repository
- Virtual Formulary
- Cancer Clinical Investigator Team Leadership Awards

# NCI-MATCH Testing and Enrollment as of 6/18/17




**6398 patients with tumor samples (N=6000)**

**5482 patients had received their test results**

**983 had a gene abnormality matching an available treatment**

And proceeded to be further evaluated for the specific eligibility for the arm to which they matched

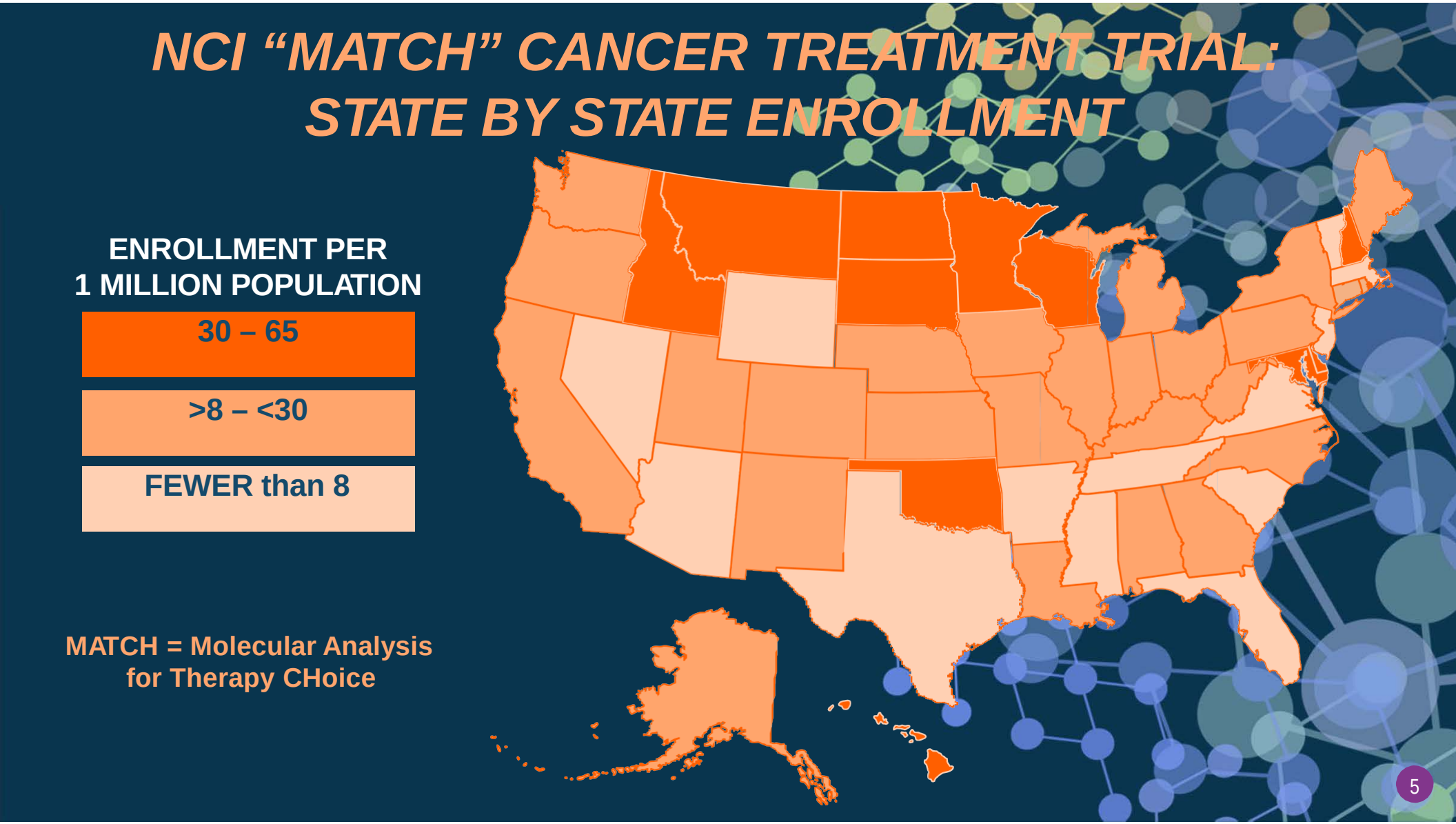
**660 patients had enrolled for treatment**

**NOTE: These are strictly numbers reflecting a point in time and cannot be used to calculate overall rates; some are assigned and still in evaluation for eligibility for an arm; estimated 72% of those assigned will enroll**

# Current:  as of June 18, 2017

- **25 treatment arms; ≈ 50% fully accrued; ≈ 25% well on the way; ≈ 25% will need additional accrual from 'rare variant study'**
- **Assay success rate 94%**
- **Median assay turnaround time 16 days**
- **Toxicity acceptable**
- **Objective responses have been observed**

# *NCI "MATCH" CANCER TREATMENT TRIAL: STATE BY STATE ENROLLMENT*



## *States with Enrollment of more than 30 patients per 1 Million Population*

- Delaware
- Hawaii
- Idaho
- Maryland
- Minnesota
- Montana
- New Hampshire
- North Dakota
- Oklahoma
- South Dakota
- Wisconsin

# NCI-MATCH Expanded to 25 Arms May 31, 2016

| Arm / Target | Drugs(s) |
|---|---|
| A EGFR mut | Afatinib |
| B HER2 mut | Afatinib |
| C1 MET amp | Crizotinib |
| C2 MET ex 14 sk | Crizotinib |
| E EGFR T790M | AZD9291 |
| F ALK transloc | Crizotinib |
| G ROS1 transloc | Crizotinib |
| H BRAF V600 | Dabrafenib+trametinib |
| I PIK3CA mut | Taselisib |
| N PTEN mut | GSK2636771 |
| P PTEN loss | GSK2636771 |
| Q HER 2 amp | Ado-trastuzumab emtansine |

| Arm / Target | Drug(s) |
|---|---|
| R BRAF nonV600 | Trametinib |
| S1 NF1 mut | Trametinib |
| S2 GNAQ/GNA11 | Trametinib |
| T SMO/PTCH1 | Vismodegib |
| U NF2 loss | Defactinib |
| V cKIT mut | Sunitinib |
| W FGFR1/2/3 | AZD 4547 |
| X DDR2 mut | Dasatinib |
| Y AKT1 mut | AZD 5363 |
| Z1A NRAS mut | Binimetinib |
| Z1B CCND1,2,3 amp | Palbociclib |
| Z1D dMMR | Nivolumab |
| Z1I BRCA 1/2 | AZD1775 |

Red = accrued 35 patients;

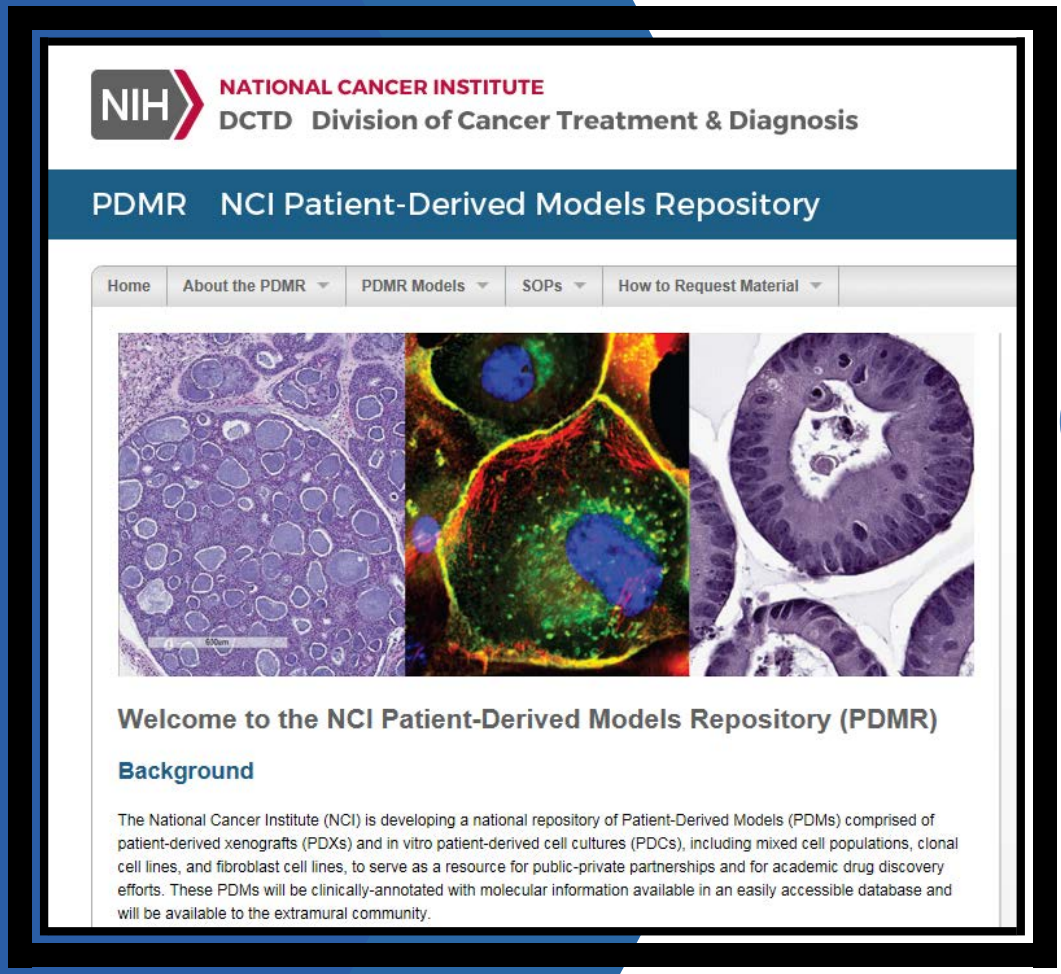
Green = nearing 35 patient

## Arms added: March 13, 2017

- EAY131-J: Herceptin + Perjeta/HER2 Amp **(to follow Arm Q)**.
- EAY131-L: MLN0128/mTOR Mutations (**New target**)
- EAY131-M: MLN0128/TSC1/TSC2 Mutations (**New target**)
- EAY131-Z1C: Palbociclib/CDK4/CDK6 Amplification (**New target**)
- EAY131-Z1E: Loxo 101/NTRK Fusions (**New target**)
- EAY131-Z1I: AZD1775/BRCA1, BRCA2 mutations ***(New target)***

# Rare variant initiative (Began May 2017)

- Several arms are not expected to fill even with sequencing 6000 patient tumors, due to the rarity of the variant in the population
- However, good evidence exists these variants are drivers and may respond to drugs in NCI MATCH
- Tumor sequencing is now more commonly done in clinical practice
- Enrichment: Initially, four additional CLIA certified labs will participate in finding these patients and letting their doctors know they may be eligible for NCI MATCH
  - 2 commercial labs
    - Foundation Medicine Inc
    - Caris
  - 2 clinical labs (using their own, non-MATCH assay)
    - MD Anderson Cancer Center
    - Memorial Sloan Kettering Cancer Center
  - Results will be verified with the MATCH assays retrospectively
  - Soon, a process for qualifying other commercial and academic sequencing labs will be posted to encourage additional accrual to this phase of NCI-MATCH

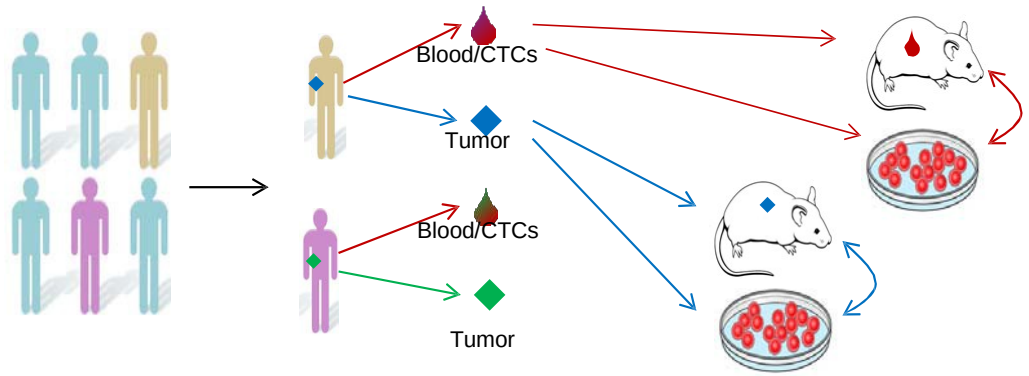



# NCI's Patient-Derived Models Repository (PDMR): Open for 6 weeks

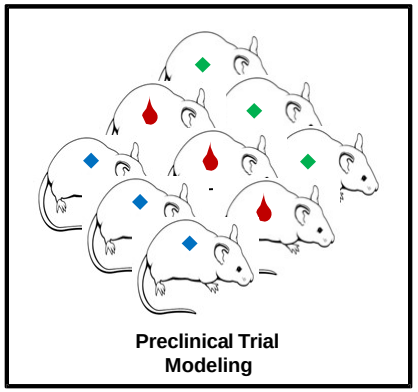
***https://pdmr.nci.gov***

# NCI Patient-Derived Models Repository: Multiple Avenues for Discovery

Develop PDX Models and PDC (Tumor & Fibroblast) Lines
DNA, RNA, Protein, WES, RNASeq, Targeted Sequencing

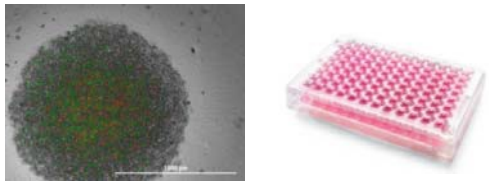



Tumor/Patient Heterogeneity

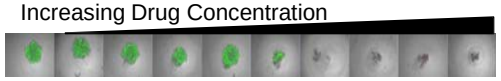


**Preclinical Trial Modeling**

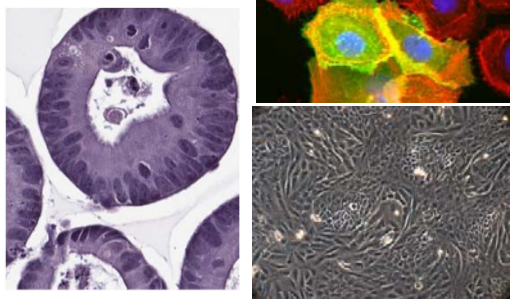
**3D Culture, 3D Pharmacodynamics**



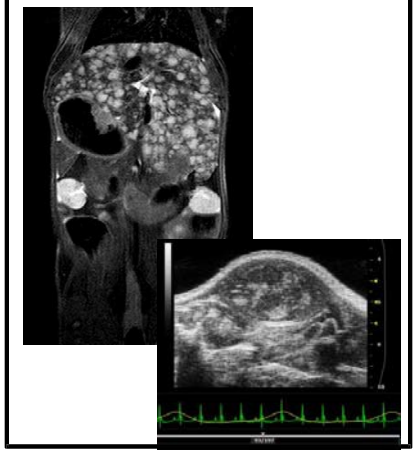
Increasing Drug Concentration



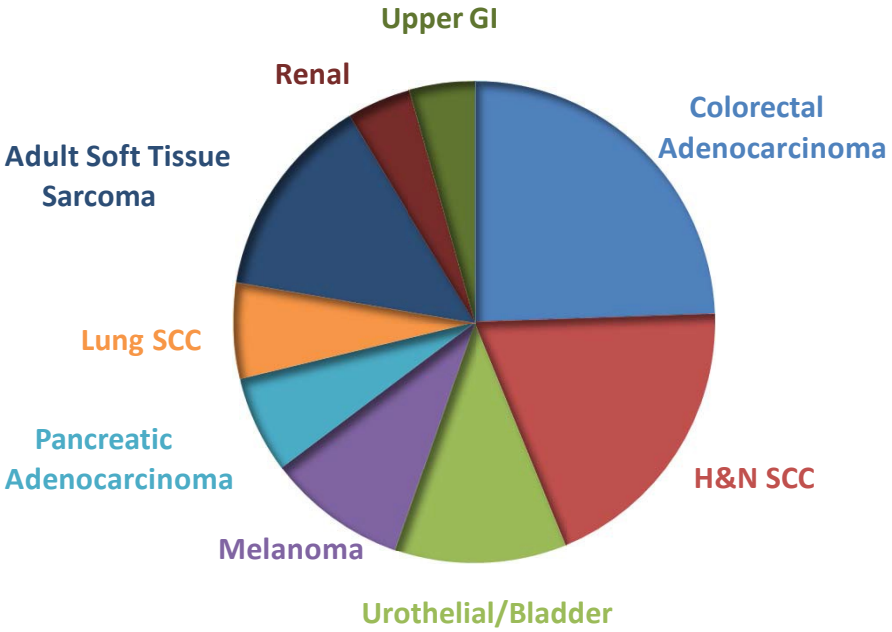
**2D and Organoid Cultures**



**Live Tumor Imaging**



# NCI Patient-Derived Models Repository (PDMR) Initial Distribution Types




- PDX Pathology Confirmed
- Whole Exome Sequence, NCI Cancer Gene Panel, and RNASeq Available
- Human Pathogen Screening and STR Profile Available
- Confirmed Re-growth from Cryopreserved Fragments

| Distribution Groups (N=100 Models) |
|---|
| **Colorectal Adenocarcinoma** |
| **Head & Neck Squamous Cell Carcinoma**<br>• Pharyngeal, Laryngeal, Lip/oral cavity, NOS |
| **Urothelial/Bladder** |
| **Melanoma** |
| **Pancreatic Adenocarcinoma** |
| **Lung Squamous Cell Carcinoma** |
| **Adult Soft Tissue Sarcoma**<br>• Ewings, Leiomyosarcoma, Malignant fibro. histiocytoma, Fibrosarcoma, Non-Rhabdosarcoma NOS, Rhabdosarcoma NOS |
| **Renal** |
| **Upper GI**<br>• Stomach, Sm. Intest, GIST, Appendiceal |

# NCI Virtual Drug Formulary

- Access to investigational drugs for investigator initiated studies is difficult and time consuming, often the cost-benefit of negotiating an agreement with a Pharmaceutical Collaborator is prohibitive or so difficult and time consuming that the study is never initiated.
- This process is especially burdensome for multi-agent combinatorial studies, and more burdensome still when one or both of those agents are investigational and proprietary to different collaborators.
- Major roadblock to precision medicine clinical trials

# NCI Virtual Drug Formulary: Development

- Created a system within the NCI that leverages our existing mechanisms to provide PIs with Investigational agents for investigator held INDs
- The program:
  - ✓ Agent menu; 8 week turn-around time for Pharma review (approval or not) of proposals
  - ✓ Utilizes pre-existing agreements/infrastructure that current Pharmaceutical Collaborators are already familiar with
- Agents provided for both clinical and pre-clinical studies
- INDs held by investigators/institutions, not CTEP/NCI; no NCI funding for trials
- Agreement terms standardized or pre-approved so as to substantially decrease the transactional costs of study initiation; NCI funds drug distribution and tracking of trials
- Launched January 2017; As of May 2017: **26** agents from **7** companies:

  Agents: Alectinib; Atezolizumab; Bevacizumab; Cobimetinib; Durvalumab; Ensartinib; Ipilimumab; Larotrectinib; LY3039478; Mogamulizumab; Nivolumab; Obinutuzumab; Pertuzumab; Prexasertib; Savolitinib; Selumetinib;Trastuzumab; Tremelimumab; Vemurafenib; Vismodegib; Vistusertib; AZD1775; AZD5069; AZD5363; AZD8186; MEDI9447

  Companies: Bristol-Myers Squibb; Eli Lilly; Genentech; Astra-Zeneca; Kyowa Hakko Kirin; Loxo; Xcovery

# Cancer Clinical Investigator Team Leadership Awards

# Cancer Clinical Investigator Team Leadership Awards

- Recognize and support outstanding clinical investigators at NCI-designated Cancer Centers who are actively engaged in NCI-funded collaborative clinical trials.
- Promote the retention of clinical investigators in academic clinical research careers.

# Cancer Clinical Investigator Team Leadership Awards

- $60,000 per year for 2 years
- 15% effort; time protected by sponsoring institution
- Candidate nominated by NCI Cancer Center Director
- 10 to 13 new awards per year
- First awards made in 2009; 102 recipients to date
- 93% (43/46) remain at NCI-Designated Cancer Center 5 years after award

# Cancer Clinical Investigator Team Leadership Awards

Supported Activities Include, but Not Limited to:

- Engaging fellows and new faculty in collaborative clinical research efforts
- Mentoring
- Organizing courses, lecture/seminar series, educational sessions, or workshops related to clinical trials
- Participating on cancer center committees related to clinical trials
- Developing a clinical trial
- Designing and implementing initiatives to better coordinate, support and integrate clinical trials efforts at the institution

# Cancer Clinical Investigator Team Leadership Awards

## Eligibility

- Engaged in conducting NCI-funded cancer clinical trials
- Practicing at least 3 years but no more than 8 years post-fellowship
- Currently practicing in the oncology clinical setting; board certified
- Full-time faculty member, assistant or associate professor level
- Physician or oncology nurse, clinical psychologist, or similarly qualified clinician with a doctoral degree

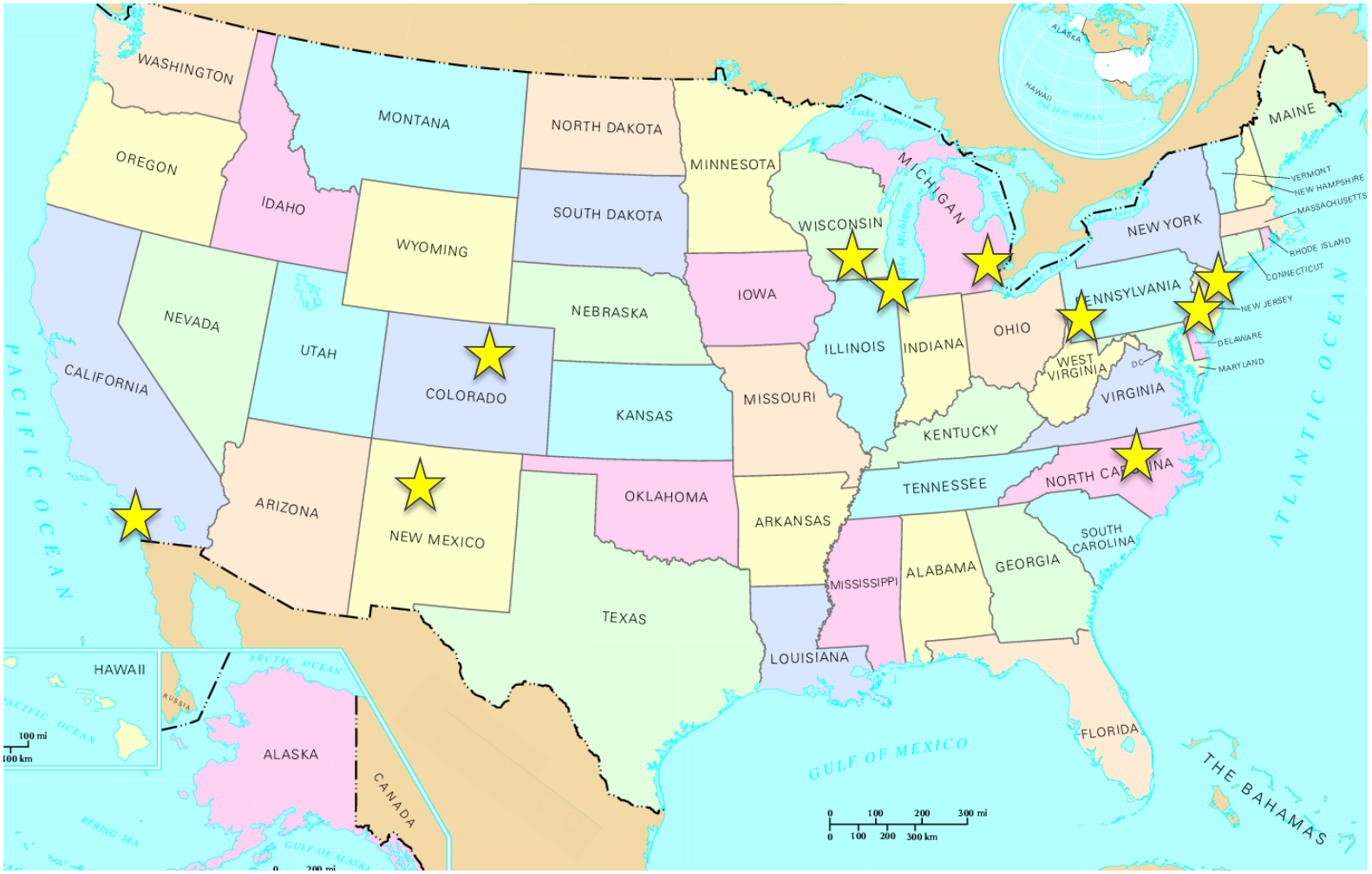
# 2017 Cancer Clinical Investigator Team Leadership Award Recipients

# Cancer Clinical Investigator Team Leadership Awards

## 2017 Recipients' Focus Areas

- Breast cancer
- Gastrointestinal cancers
- Genitourinary cancers
- Gynecological cancers
- Leukemia
- Melanoma
- Palliative care/symptom science
- Inclusion of underserved populations in clinical trials

# 2017 CCITLA Recipients

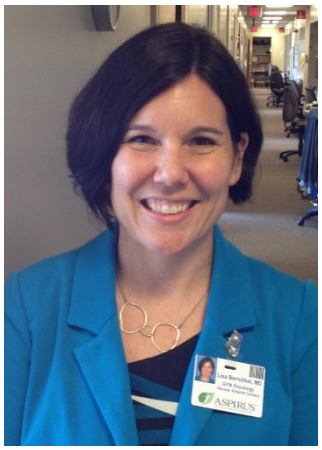


# 2017 CCITLA Recipients

**Ajjai Alva, M.D., M.S.**

**University of Michigan Comprehensive Cancer Center**

**Focus: Genitourinary cancers**



**Lisa Barroilhet, M.D.**

**University of Wisconsin Carbone Cancer Center**

**Focus: Gynecologic cancers**

# 2017 CCITLA Recipients

**Ursa Brown-Glaberman, M.D.**

**University of New Mexico Comprehensive Cancer Center**

**Focus: Breast cancer**

**Shira Dinner, M.D.**

**Robert H. Lurie Comprehensive Cancer Center**
**Northwestern University**

**Focus: Leukemia**

# 2017 CCITLA Recipients


**Jean Hoffman-Censits, M.D.**

**Sidney Kimmel Cancer Center**
**Thomas Jefferson University**

**Focus: Bladder and prostate cancers**

**Kevin Kalinsky, M.D., M.S.**

**Herbert Irving Comprehensive Cancer Center**
**Columbia University**

**Focus: Breast cancer**

# 2017 CCITLA Recipients

**Christopher Lieu, M.D.**

**University of Colorado Comprehensive Cancer Center**

**Focus: Colorectal cancer**

**Rahul Parikh, M.D., Ph.D.**

**University of Pittsburgh Cancer Institute**

**Focus: Bladder cancer**

# 2017 CCITLA Recipients

**Eric Roeland, M.D.**

**Moores Comprehensive Cancer Center**
**University of California, San Diego**

**Focus: Symptom intervention / palliative care (all cancers), gastrointestinal cancers**

**April Salama, M.D.**

**Duke Cancer Institute, Duke University Medical Center**

**Focus: Melanoma**

# Congratulations to the 2017 NCI Cancer Clinical Investigator Team Leadership Award Recipients


**www.cancer.gov** **www.cancer.gov/espanol**