Division of Cancer Treatment and Diagnosis (DCTD)

Presented By: Michael Difilippantonio, Ph.D.

September 23, 2016
Overview of DCTD
Mission and Purpose

To improve the lives of cancer patients by enabling the scientific transition from basic research to advanced clinical studies of cancer diagnostics and therapeutics.
Division of Cancer Treatment and Diagnosis (DCTD)
James Doroshow, MD – Director
Toby Hecht, PhD – Deputy Director

- Biostatisticians, Clinical Trial Design, Data Analysis

Cancer Diagnosis Program (CDP) – Barbara Conley, MD
- Clinical Assays (diag., prog., stratification), Biospecimens

Cancer Imaging Program (CIP) – Paula Jacobs, PhD
- Imaging Modalities (PET, SPEC, NMR, etc)
- Applications (diag., surgical margins, Tx response, drug targeting)

Cancer Therapy Evaluation Program (CTEP) – Jeff Abrams, MD
- Phase 1 – Phase 3 clinical trials, invest. agents, new indications, combination studies
Division of Cancer Treatment and Diagnosis (DCTD)

Developmental Therapeutics Program (DTP) – Jerry Collins, PhD

- Drug discovery, pre-clinical development (pharm., ADMET, chem., formulation, PD, Natural Products, biologics, etc)

Radiation Research Program (RRP) – Norman Coleman, MD

- Technical advances, radiation / drug synergy

Translational Research Program (TRP) – Toby Hecht, PhD

- SPORE Grants

Office of Cancer Complimentary and Alternative Medicine (OCCAM) – Jeffrey White, MD

- Traditional Chinese medicine (TCM), herbal, yoga, meditation, etc.
DCTD Contributions to FDA Approved Drugs
## FDA Approved Therapeutics Developed with Assistance from NCI in the Past 15 Years

<table>
<thead>
<tr>
<th>Year</th>
<th>Agent</th>
<th>Role of NCI</th>
<th>Mechanism of Support</th>
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</thead>
<tbody>
<tr>
<td>2015</td>
<td>Dinutuximab (ch14.18 ab)</td>
<td>Produced antibody; conducted pivotal trials</td>
<td>FNLCR biologics facility; NCI Cooperative Grant</td>
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<tr>
<td>2010</td>
<td>Sipuleucel (Provenge®)</td>
<td>Oversaw production</td>
<td>National Cooperative Drug Discovery Grant</td>
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<tr>
<td>2010</td>
<td>Eribulin</td>
<td>Natural product discovery; screening; formulation of clinical product; animal efficacy testing; clinical candidate selection; first-in-human trial</td>
<td>FNLCR labs; Analytical, Formulation, PK, Toxicology contracts; RO1 grant; U01 grant</td>
</tr>
<tr>
<td>2009</td>
<td>Pralatrexate</td>
<td>RAID project; NCI produced GMP bulk drug</td>
<td>GMP bulk drug mfg. contract</td>
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<tr>
<td>2009</td>
<td>Romidepsin (Depsipeptide)</td>
<td>Developed safe human dosing schedule in large animals; PK and Tox; produced drug; conducted first-in-human trials in NIH CC</td>
<td>FNLCR animal facilities; Pharmacology, Toxicology, Drug Production contracts</td>
</tr>
<tr>
<td>2004</td>
<td>Cetuximab</td>
<td>Produced first lots for imaging and chimeric clones</td>
<td>Contracts; Cooperative Drug Discovery Grant</td>
</tr>
<tr>
<td>2004</td>
<td>5-Azacytidine</td>
<td>Pre-clinical molecular pharmacology; produced pre-clinical / clinical drug supply; conducted pivotal trial</td>
<td>FNLCR Labs; Contracts; U01 Grants</td>
</tr>
<tr>
<td>2003</td>
<td>Bortezomib</td>
<td>Extensive analog screening; MOA and PD studies; PK &amp; Tox; clinical formulation</td>
<td>FNLCR Labs; Formulation, PK, Toxicology contracts</td>
</tr>
<tr>
<td>2000</td>
<td>Temozolomide</td>
<td>Scale up synthesis and clinical formulation</td>
<td>Bulk drug and Formulation contracts</td>
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## Pivotal NCI/CTEP-sponsored Group Trials Contributing to FDA Approved Indications for New Oncology Agents

<table>
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<tr>
<th>Year</th>
<th>Agents</th>
<th>Group</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Depsipeptide (Istodax®)</td>
<td>ECOG, Intergroup</td>
<td>Gloucester Pharmaceuticals, Inc.</td>
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<tr>
<td>2007</td>
<td>Lapatinib (Tykerb®) Deoxycoformycin (Pentostatin®)</td>
<td>NCCTG, CALGB, Intergroup</td>
<td>GSK Bedford Labs</td>
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<tr>
<td>2006</td>
<td>Dasatinib (Sprycel®) Sunitinib (Sutent®) Pegaspargase (Oncaspar®)</td>
<td>SWOG, Intergroup ECOG, Intergroup</td>
<td>BMS Pfizer Enzon</td>
</tr>
<tr>
<td>2005</td>
<td>Lenalidomide (Revlimid®) Nelarabine (Arranon®) Sorafenib (Nexavar®)</td>
<td>ECOG, Intergroup COG, CALGB ECOG, Intergroup</td>
<td>Celgene GSK Bayer / Onyx</td>
</tr>
<tr>
<td>2004</td>
<td>5-Azacytidine (Vidaza®) Bevacizumab (Avastin®) Erlotinib (Tarceva®) Taxotere (Doxetaxol®)</td>
<td>CALGB ECOG. Intergroup NCCTG, Intergroup SWOG</td>
<td>Celgene Genetech Genentech / OSI Sanofi-Aventis</td>
</tr>
<tr>
<td>2002</td>
<td>Oxaliplatin (Eloxatin®)</td>
<td>NCCTG, Intergroup</td>
<td>Sanofi-Aventis</td>
</tr>
<tr>
<td>2001</td>
<td>Imatinib mexylate (Gleevec®) Letrozole (Femara®)</td>
<td>COG, SWOG NCIC, Intergroup</td>
<td>Novartis Novartis</td>
</tr>
<tr>
<td>2000</td>
<td>Arsenic trioxide (Trisenox®)</td>
<td>CALGB</td>
<td>Cell Therapeutics</td>
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</table>
NCI Experimental Therapeutics (NExT) Program: One Goal, Several Mechanisms
Transformation of the NCI Therapeutics Pipeline

NIH Roadmap
MLPCN

Cancer Centers

SPORE

RO1/P01

Biotech & Pharma

MTF / DDC

Imaging / IDG

RAID

DDG

The NCI Experimental Therapeutics (NExT) Pipeline:
Target discovery through early stage clinical trials

Harmonize Activities into Single Pipeline
NOT A GRANT PROGRAM

- Clear path to clinic/patient benefit
- Provides access to NCI resources and drug development expertise
- Integrates a variety of prior decentralized and uncoordinated programs
- Simple application
- Applicant PI is actively involved since it is their project
NExT Resources Currently Support

- Investigational drugs, biologics and NP’s
- Investigational imaging agents
- Academic, biotech, pharma and government projects
- HTS, Hit-to-Lead, Lead Optimization, Clinical Candidate, Phase 0, 1 and 2 clinical trials

NOT basic research
Beryllium Discovery Corp.
University of California, San Francisco
Evotec Compound Management
SRI International
Pharmanor
Sanford Burnham Prebys Medical Discovery Institute
The Scripps Research Institute
Vala Sciences Inc.

University of Pittsburgh
SAMDI Tech
University of Chicago
Purdue University
University of New Mexico
Arizona State University
Southern Research Institute

Albany Molecular Research Inc.
Xtal BioStructures Inc.
Reaction Biology Corp.
NCATS Chemical Genomics Center
University of North Carolina at Chapel Hill
Vanderbilt University
Emory University
Torrey Pines Institute for Molecular Studies

NExT Discovery Engine
Chemical Biology Consortium
FNLCR sub-contracts

NIH NATIONAL CANCER INSTITUTE
PK/PD Modeling
Tox/Safety Pharmacology
GMP Scale-Up

Imaging supported by Cancer Imaging Program

Development and validation of PD assays during preclinical stages is supported by the Pharmacodynamics Assay Development & Implementation Section (PADIS) and during clinical stages by the National Clinical Target Validation Laboratory (NCTVL).

Clinical Assay Development Program (CADP) development and validation of clinical assays (including diagnostic).
- Currently sponsors over 100 INDs
- Approx. 11,000 registered investigators at over 3,300 institutions
- Over 750 active protocols
- 150-250 new protocols/year
- Approx. 30,000 patients accrued/year
- Over 80 collaborative agreements (CRADAs, CTAs, and CSAs) with pharmaceutical companies (Collaborators)
Role of FNLCR in NCI Therapeutics Development Program

- **Natural Products & Medicinal Chemistry**
- **Biopharmaceutical Development & New Animal Models**
- **Small Animal Imaging & Imaging Drug Development**
- **Pharmacodynamics**
- **Genomic Characterization**

**Targets**
- High risk targets
- Investigational imaging agents
- Investigational drugs, biologics, natural products
- Unmet medical needs (rare cancers, pediatric tumors)
- Academic & Biotech & Pharma projects

**Therapeutics**
What are we looking for?

- **Program Directors (pre-clinical development)**
  - Immunotherapy
  - Molecular Pharmacology
- **Program Directors (clinical development)**
  - Clinical Assays
  - Clinicians

* Supervisory and non-supervisory positions available