Drug Project Team Basics

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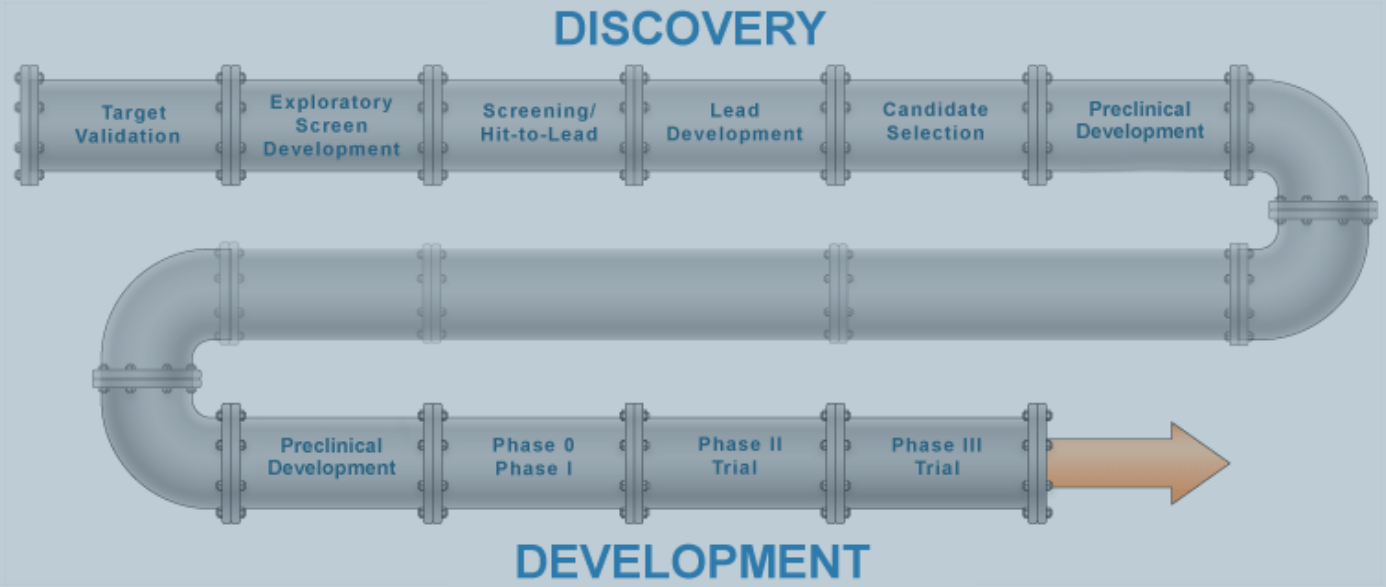
Overall Process of NCI-Sponsored Drug Development

NCI: Partnerships with Industry and Academia for Cancer Drug Development

- **For over seven decades,** NCI has done drug development and discovery in the public interest.
- **For over five decades**, NCI has coordinated relationships between Industry and Academia to help develop new cancer drugs.

- In the current iteration of this effort, two programs run in sequence to manage a portfolio of partnerships between NCI and Industry or Academia.
- **NCI Experimental Therapeutics (NExT) Program** is the program that selects agents for NCI-sponsored pre-clinical and clinical development.



- The **Experimental Therapeutics Clinical Trials Network (ETCTN)** is the clinical trials network that performs clinical studies of agents that are approved through NExT.
- In these partnerships, NCI
  - Assumes the regulatory responsibility for the trials (IND holder);
  - Pays for the clinical trials through cooperative grants (UM1) to ETCTN clinical trial sites;
  - Works with ETCTN investigators and industry/academia partners to formulate the clinical development plan for the agent.

NCI: Advantages for Industry to Co-Develop Agents with CTEP through the NCI Experimental Therapeutics Program (NExT)

- CTEP has **access** to novel agents from industry competitors, and therefore, can act as an honest broker for novel drug combination studies.
- Industry realizes that there are potential therapeutic indications that **do not have high enough priority** to compete for limited corporate resources.
- CTEP can **expend** public funds for clinical trials and regulatory support to advance the development of agents owned by industry.
- CTEP has a **network** of experienced early-phase clinical trial investigators engaging its centralized clinical trial support systems.
- CTEP **invests** in correlative science studies to explore the pharmacodynamics of agents in clinical studies.

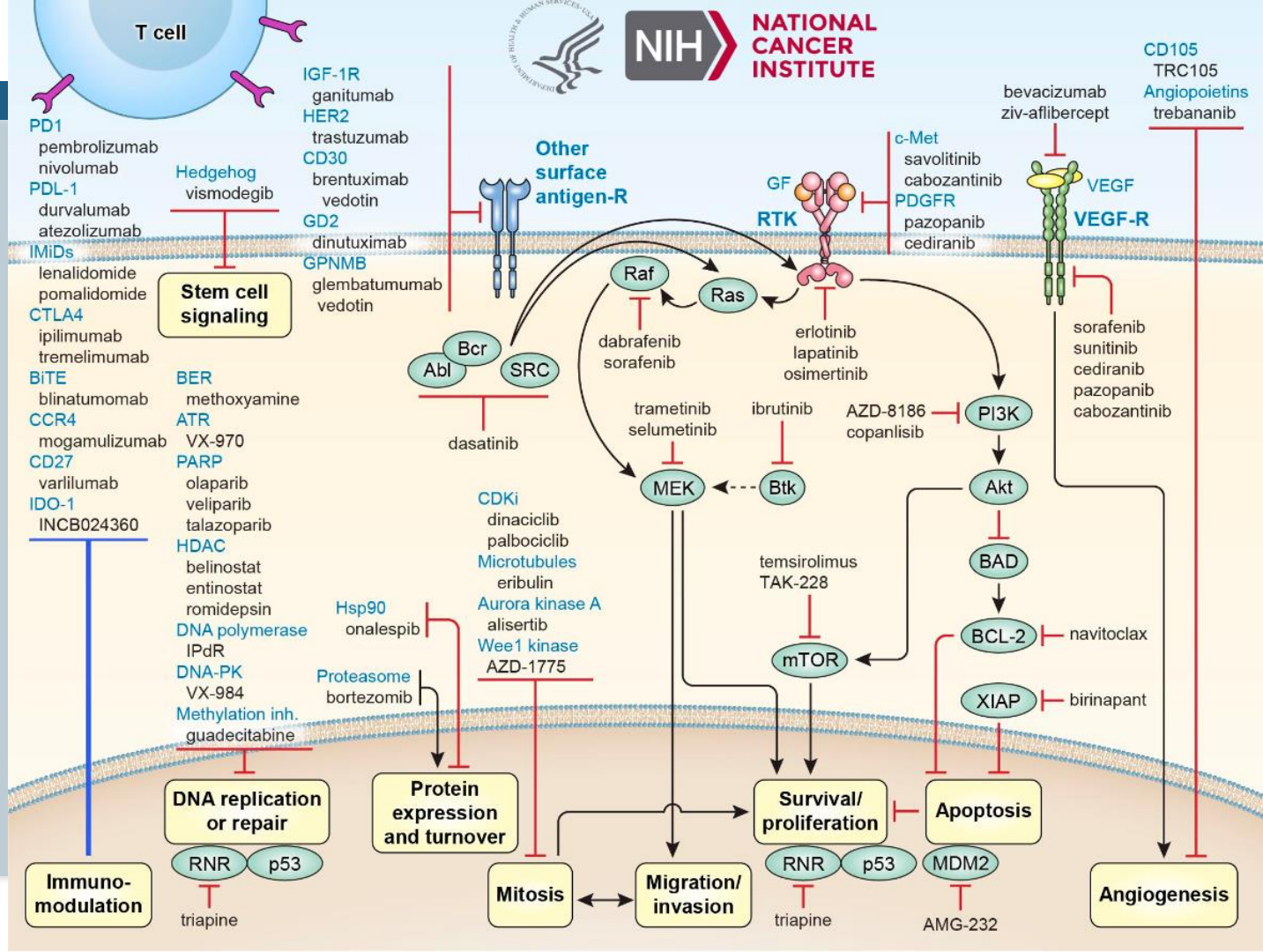
NCI: Why Extend Effort to Assist Industry Develop Its Agents

- NCI recognizes that there is a **significant public interest** in finding indications for new oncology drugs beyond those that may be the most profitable.

- NCI can **advance the understanding of cancer biology and treatment** through carefully designed clinical trials and through the correlative studies that are frequently and extensively incorporated into CTEP-sponsored ETCTN trials.

CTEP: Current Portfolio

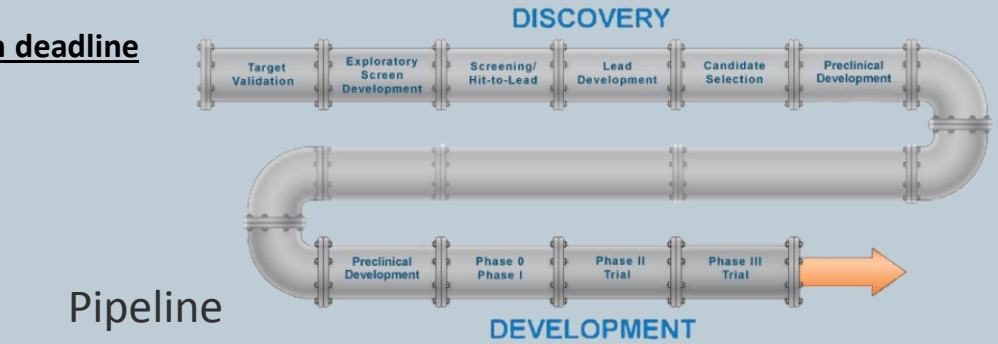
- 72 active agents under cooperative research and development agreement (CRADA)
- https://ctep.cancer.gov/industryCollaborations2/agreements_agents.htm



Overall Process of NCI Experimental Therapeutics Program

CTEP: Overall Process of NCI Experimental Therapeutics (NExT) Program

- Pharmaceutical Company Q applies for NCI CTEP collaboration through the **NExT program** to help develop Drug X
- The NExT program application proposes an envisioned collaboration in which NCI-sponsored clinical trials test Drug X **in combination with specific CTEP IND agents** (entering Discovery or Development phases of the NExT pipeline)
- If Drug X is approved by the NExT program and ready for clinical development, an internal NCI committee discusses a **preliminary internal clinical development plan**, which is reviewed and approved by another internal NCI committee.
- If the preliminary clinical development plan is endorsed, two next steps occur:
  - A Drug X **Project Team** is formed
  - **Cooperative Research And Development Agreement (CRADA)** negotiations start with Pharmaceutical Company Q
    - Both processes have a **six (6) month deadline**



Pipeline

Project Team Basics

Cancer Therapy Evaluation Program (CTEP)

CTEP: Project Team Basics (1)

- Leading extramural experts, together with CTEP medical officers & staff, formulate drug clinical development plan(s).
  - Though previous clinical development plans (NExT application and preliminary internal plan) may be referenced, the Drug Project Team starts from a 'clean' slate.
  - There are three major benefits:

Involves extramural scientific and clinical experts in planning

Overlaps Project Team planning with CRADA negotiations to shorten timeline

Speeds writing process and review of Project Team Letters of Intent (LOIs)

CTEP: Project Team Basics (2)

- Project Teams are 'quick'—intended to be in existence for 8-12 weeks.
  - Project Teams have intramural and extramural participation.
  - Four extramural roles are recruited to Project Teams:

Clinician Scientist → Translational Scientist → Pharmacologist → Cancer Biologist

  - Project Team Leadership involves a CTEP Medical Officer and two (2) extramural scientists.
  - Project Team meetings are held by Webinar.
  - Being selected to a Project Team requires attendance at all planned whole-team meetings.

CTEP: Project Team Basics (3)

- The concept is to recruit the most qualified experts to develop the initial development plan—only individuals, *and not teams*, may apply.
  - An exception is when an Early Career Investigator applies with a mentor.
  - For Early Career Investigators, the most important advice is—*apply with a mentor*. It is highly unlikely that an Early Career Investigator could be competitive in Project Team selection without a mentor.
  - For potential mentors, the most important advice is—*apply with an Early Career Investigator*. Preference has been given to mentor/Early Career Investigator combinations, as mentorship & training are important NCI CTEP programmatic goals.

93% (14/15) of the last three Project Team trials are led by Mentor/Early Career Investigators

CTEP: Project Team Basics (4)

- The Project Team Member Application (PTMA) recruits participants to a Project Team.
  - The PTMA is very simple form, and requires only the attachment of your NIH Biosketch.
  - Customize your personal statement to the Drug Project Team application (i.e., why you should be selected).
- Project Team work product at its end is a drug clinical development plan to be presented to the Investigational Drug Steering Committee (IDSC), typically in person at a face-to-face meeting or webinar.
- Clinician scientists should anticipate being the Principal Investigator (PI) of clinical trials that arise in the process.
- Translational and basic scientists may also become members of the study teams for these trials.
- ETCTN UM1 supplement grants may be available for preclinical studies or biomarker assay development.

Project Team Workflow

Cancer Therapy Evaluation Program (CTEP)

CTEP: Project Team Selection and Workflow

Step **1**

Project Team Formation

Step **1.1**

Project Team Member Applications Submitted

Available Roles:

A. Clinician Scientist
B. Translational Scientist
C. Pharmacologist
D. Cancer Biologist

Step **1.2**

CTEP Medical Officer Reviews Applications

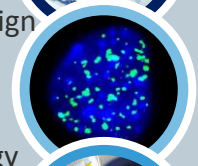
Step **1.3**

CTEP Selects Team Members

Step **1.4**

Initial Project Team WebEx Calls

Design



Biology

Pharmacology

Step **1.5**

Individual Project WebEx Calls

Step **1.6**

Investigational Drug Steering Committee Reviews Individual Projects

CTEP: Project Team Roles—Clinician Scientist(s)

- Expected to actively participate in developing a comprehensive plan to be endorsed by the Investigational Drug Steering Committee (IDSC)
  - Clinician Scientists (i.e., Principal Investigators) will present clinical information to the IDSC
- Expected to lead or co-lead clinical trials that come out of the Project Team planning process
  - Not guaranteed – selected clinical investigators that do not participate in team activities will be replaced
- Clinician scientists should be from ETCTN-affiliated sites

CTEP: Project Team Roles—Translational Clinical Scientist(s)

- Expected to help develop biomarker endpoints for clinical studies
- Expected to help select appropriate technology platforms, and to work out many details of biomarker selection and test qualification with the Cancer Diagnosis Program (CDP) and its Biomarker Review Committee (BRC)
- May be eligible to apply for supplemental UM1 grant funds for selected projects
- Have the opportunity to incorporate the same biomarkers on the same platforms in multiple trials
- Translational clinical scientists do not need to be from ETCTN-affiliated sites

CTEP: Project Team Pharmacologist(s)

- Expected to help develop pharmacokinetic endpoints for clinical studies
- Expected to help select appropriate pharmacokinetic technology platforms and performance sites
- Expected to work out many details of possible drug-drug or radiation-drug interactions that might justify phase 1 clinical trials
- May be eligible to apply for supplemental UM1 grant funds for selected projects
- Have the opportunity to incorporate the pharmacokinetics on the same platforms in multiple trials
- Pharmacologists should be from ETCTN-affiliated sites

CTEP: Project Team Cancer Biologist(s)

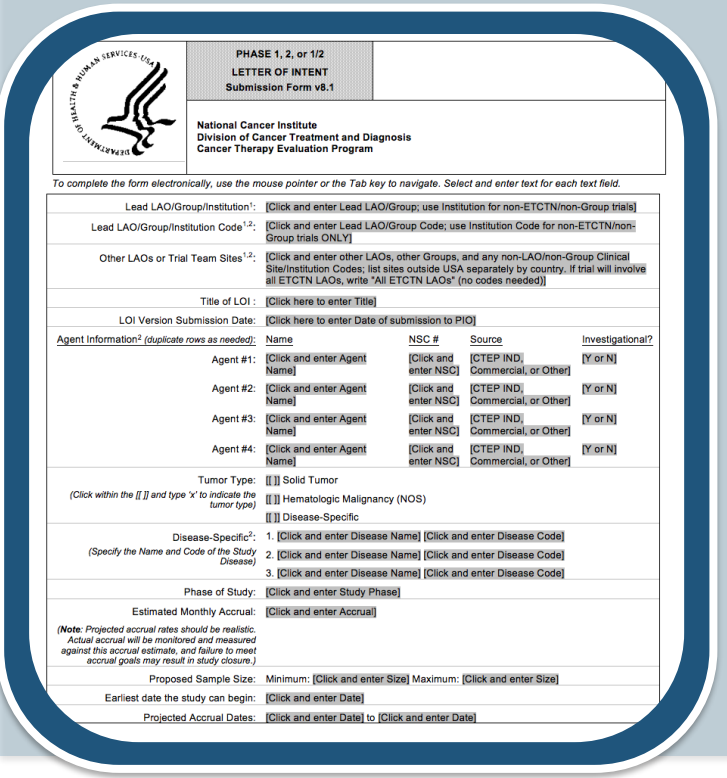
- Expected to educate the team about the basic science behind the drug
- Expected to help guide trial design based on underlying knowledge of mechanism of action of the agent
- Expected to help guide biomarker selection
- May perform experiments to help guide deliberations – will have access to NCI CTEP portfolio agents
- May be eligible to apply for supplemental UM1 grant funds for selected projects.
- Cancer Biologists do not need to be from ETCTN-affiliated sites

Project Team Work Product

Cancer Therapy Evaluation Program (CTEP)

CTEP: Centralized Letter of Intent (LOI) Pathway Submission

- There are two paths for CTEP support of clinical development ideas—Project Team LOIs or Unsolicited Trial LOIs.



PHASE 1, 2, or 1/2
LETTER OF INTENT
Submission Form v8.1

National Cancer Institute
Division of Cancer Treatment and Diagnosis
Cancer Therapy Evaluation Program

To complete the form electronically, use the mouse pointer or the Tab key to navigate. Select and enter text for each text field.

Lead LAO/Group/Institution[1]:	[Click and enter Lead LAO/Group; use Institution for non-ETCTN/non-Group trials]
Lead LAO/Group/Institution Code[1,2]:	[Click and enter Lead LAO/Group Code; use Institution Code for non-ETCTN/non-Group trials ONLY]
Other LAOs or Trial Team Sites[1,2]:	[Click and enter other LAOs, other Groups, and any non-LAO/non-Group Clinical Site/Institution Codes; list sites outside USA separately by country. If trial will involve all ETCTN LAOs, write "All ETCTN LAOs" (no codes needed)]
Title of LOI :	[Click here to enter Title]
LOI Version Submission Date:	[Click here to enter Date of submission to PIO]

Agent Information[2] *(duplicate rows as needed)*:	Name	NSC #	Source	Investigational?
Agent #1:	[Click and enter Agent Name]	[Click and enter NSC]	[CTEP IND, Commercial, or Other]	[Y or N]
Agent #2:	[Click and enter Agent Name]	[Click and enter NSC]	[CTEP IND, Commercial, or Other]	[Y or N]
Agent #3:	[Click and enter Agent Name]	[Click and enter NSC]	[CTEP IND, Commercial, or Other]	[Y or N]
Agent #4:	[Click and enter Agent Name]	[Click and enter NSC]	[CTEP IND, Commercial, or Other]	[Y or N]

Tumor Type: *(Click within the [[ ]] and type 'x' to indicate the tumor type)*	[[ ]] Solid Tumor [[ ]] Hematologic Malignancy (NOS) [[ ]] Disease-Specific
Disease-Specific[2]: *(Specify the Name and Code of the Study Disease)*	1. [Click and enter Disease Name] [Click and enter Disease Code] 2. [Click and enter Disease Name] [Click and enter Disease Code] 3. [Click and enter Disease Name] [Click and enter Disease Code]
Phase of Study:	[Click and enter Study Phase]
Estimated Monthly Accrual: *(Note: Projected accrual rates should be realistic. Actual accrual will be monitored and measured against this accrual estimate, and failure to meet accrual goals may result in study closure.)*	[Click and enter Accrual]
Proposed Sample Size:	Minimum: [Click and enter Size] Maximum: [Click and enter Size]
Earliest date the study can begin:	[Click and enter Date]
Projected Accrual Dates:	[Click and enter Date] to [Click and enter Date]

- The better composed an LOI, the easier it is on the ETCTN centralized protocol writing service (CPWS) to write your initial protocol and the easier it is on you to supply requested content.
- Competitive LOIs contain:

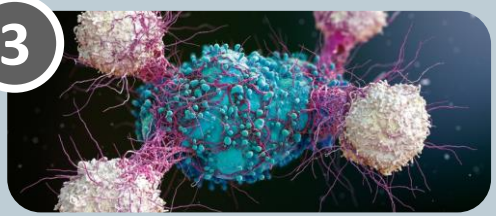
1

Test combinations in two disease-relevant cell lines

2

Test combinations in two disease-relevant xenograft models

3



Concise biomarker plans for integral, integrated, or exploratory assays inclusive of tissue, timing, funding

4

Supported experimental agent rationale in study disease cohort, with reasoned agent dose & schedule & duration

CTEP: Project Team Work Product (1)

- Project Team clinical trials are presented to the Investigational Drug Steering Committee (IDSC).
  - IDSC is an advisory committee to CTEP, meaning:
    - Recommendations are important, **but not binding;**
    - Recommendations are **generally incorporated** into proposed clinical trial Letters of Intent (LOIs).
  - The IDSC has the following expertise: drug development, clinical pharmacology, clinical immunology, clinical trial design, omics, imaging, biostatistics, patient advocacy.
  - Members include Principal Investigators (PIs) of all ETCTN UM1 grants (including pediatric oncology); this includes all PIs from multi-PI sites.
  - IDSC votes by 'secret' ballot and provides comments on Project Team proposals.

CTEP: Project Team Work Product (2)

- If approved by the Investigational Drug Steering Committee (IDSC), the overall plan is presented to another internal committee for final approval.
- If CRADA negotiations have been successfully executed, clinician scientists (i.e., principal investigators) on the Project Teams are invited to submit formal Letters of Intent (LOIs) to CTEP, submitted **within 30 days** of the date of the final approval (unless extended for preclinical data generation and review).

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