

Overview on how to submit a clinical Letter of Intent (LOI) to NCI/CTEP

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Associate Chief Investigational Drug Branch
Program Director of the ETCTN

Cancer Therapy Evaluation Program (CTEP)

Experimental Therapeutics Clinical Trials Network (ETCTN)

California Cancer Consortium Conference

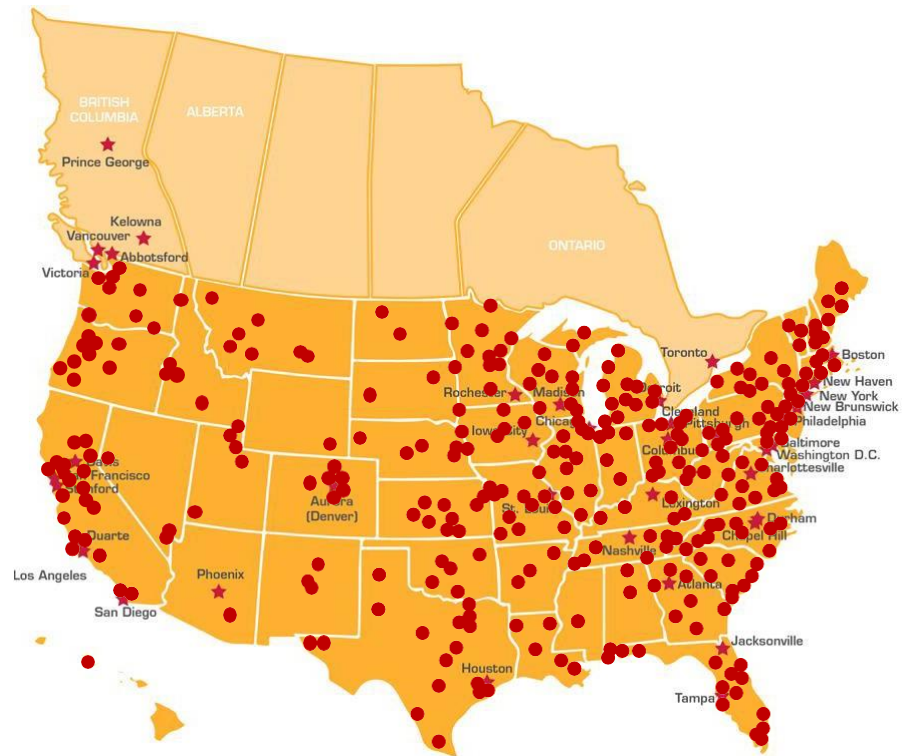
August 23-25, 2024

Pasadena, California

Goals and Objectives of the ETCTN

Cancer Therapy Evaluation Program (CTEP)

- **Research and Develop New Cancer Treatments**
 - Explore dose and schedule in early treatment trials exploring
 - Pharmacokinetics/Pharmacodynamics
 - Biologically effective dosing
 - Conduct trials of novel combination therapies
- **Study Tumor Characterization in Biomarker-driven Studies**
 - Interrogate molecular characterization: expression, sequence, and epigenetics
 - Validate biomarker assays in qualified laboratories (predictive biomarkers)
 - Incorporate functional imaging
- **Provide Enhanced Understanding of Cancer Biology**
- **Offer Education and Training for Early Career Investigators**

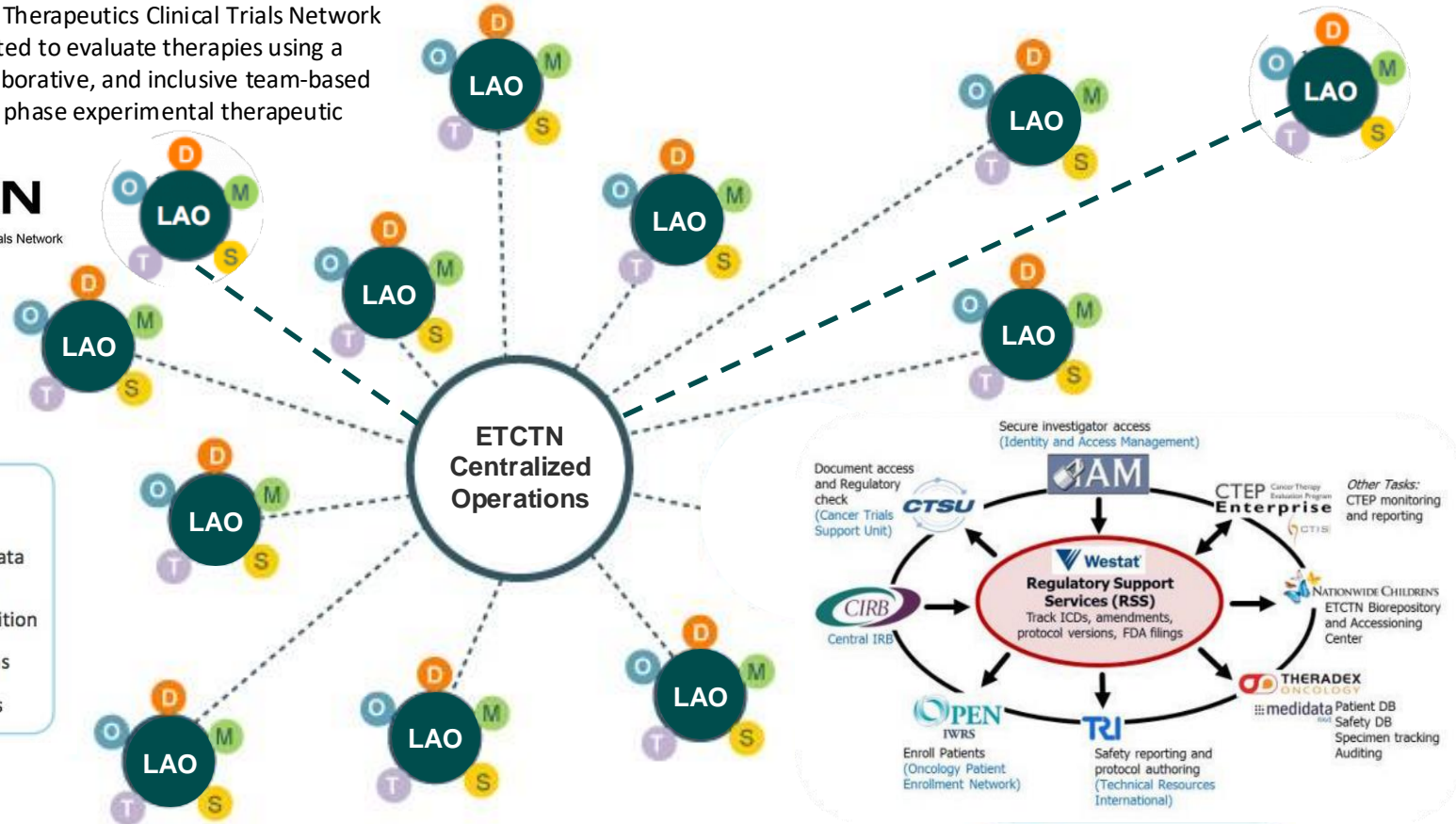


- Experimental Therapeutics Clinical Trials Network (ETCTN)
 - Studies phase 0, 1, or 2 clinical trials with biologic endpoints
 - ★ Lead Academic Organization (LAO, 12) or affiliate (41) ● Early Drug Development Opportunity Program (15)

- National Clinical Trials Network (NCTN) – cooperative groups
 - Studies randomized phase 2 or 3 clinical trials with clinical endpoints

CTEP: Experimental Therapeutics Clinical Trials Network (ETCTN) & Lead Academic Organization (LAO) infrastructure

- The Experimental Therapeutics Clinical Trials Network (ETCTN) was created to evaluate therapies using a coordinated, collaborative, and inclusive team-based approach to early phase experimental therapeutic clinical trials.



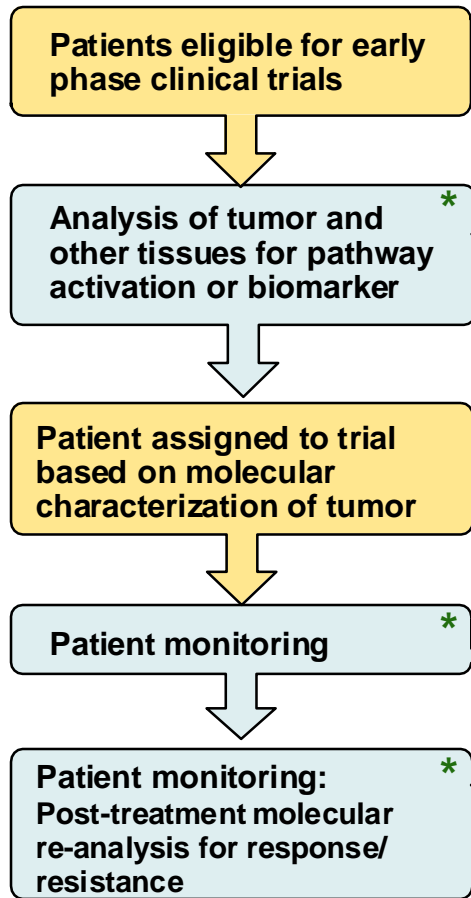
LEGEND

- O Operations
- S Statistics & Data Management
- T Tissue Acquisition
- D Disease Teams
- M Member Sites

- The objectives of the ETCTN are to:
- Conduct early clinical trials of NCI-IND agents in high priority areas of unmet medical needs
- Ensure efficient and timely activation and conduct of these clinical trials
- Integrate preclinical findings using clinical samples for biomarker analysis
- Promote collaboration among institutions and investigators
- Integrate molecular characterization, pharmacology, cancer biology, and imaging into clinical trials

***Clinical observations:**

- Clinical response**
- PK**
- Functional imaging**
- Tumor and normal tissue PD markers**
- CTCs, CECs**
- Tumor-initiating cells**



Non-clinical models for targets

Translational research with clinical models

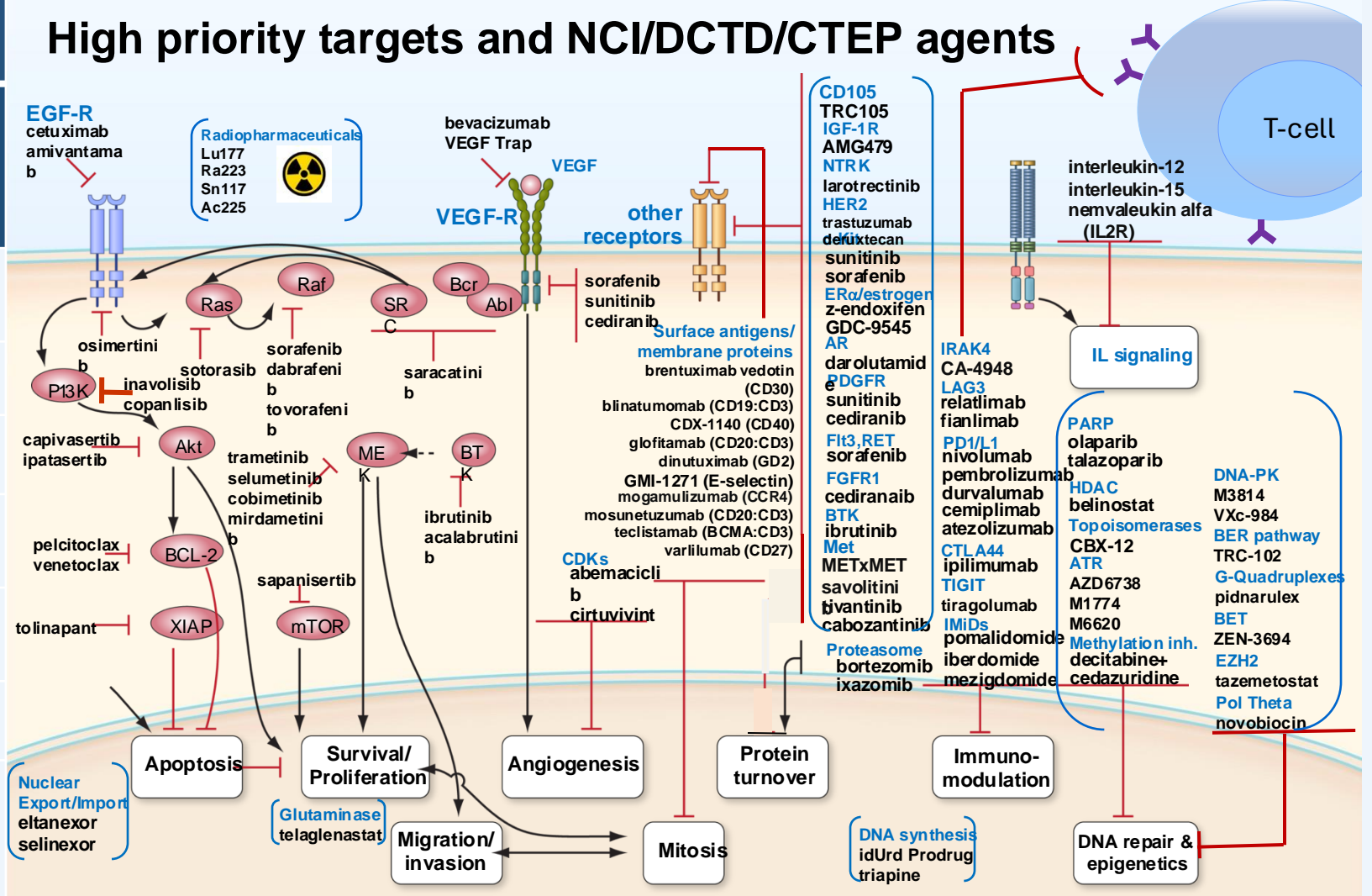
- Sequencing**
- Methylation**
- FISH**
- IHC**
- Expression array**

CTEP AGENTS

Broad range of agents addressing:

- Signal Transduction
- Cell cycle
- DNA Repair
- Apoptosis Modulation
- Epigenetic Targets
- Angiogenesis
- Immuno-modulation

High priority targets and NCI/DCTD/CTEP agents



CTEP: Project Team Basics—sets the initial clinical development and biomarker plan for a new NExT agent



Activity	Number of LOIs (%)
Project Teams	26
Letters Of Intent (LOIs) solicited from Project Teams with an Early Career Investigator	62 (83%)
LOIs with an Early Career Investigator 03.2014-9.2022	150 (48%)
Unsolicited or pre-solicitation LOIs with an Early Career Investigator	80 (45%)
Activated or transitioned ETCTN protocol with an Early Career Investigator	81 (49%)

A Day in the Life of a ETCTN Trial Proposal

Cancer Therapy Evaluation Program (CTEP)

CTEP: Centralized Letter of Intent (LOI) Pathway Submission

Path: **PROJECT TEAM** Letter of Intent (Solicited)

- There are two paths for CTEP support of clinical development ideas—Project Teams or Unsolicited Trials.

Path: **UNSOLICITED TRIAL** Letter of Intent (Unsolicited)

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/Institution¹: [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 PIG]

Agent Information ³ (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: [] Solid Tumor
 (Click within the [] and type 'x' to indicate the tumor type)
 [] Hematologic Malignancy (NOS)
 [] Disease-Specific

Disease-Specific²:
 (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: [Click and enter 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.)

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]

Competitive LOIs :



Test combinations in two disease-relevant cell lines



Test combinations in two disease-relevant xenograft models

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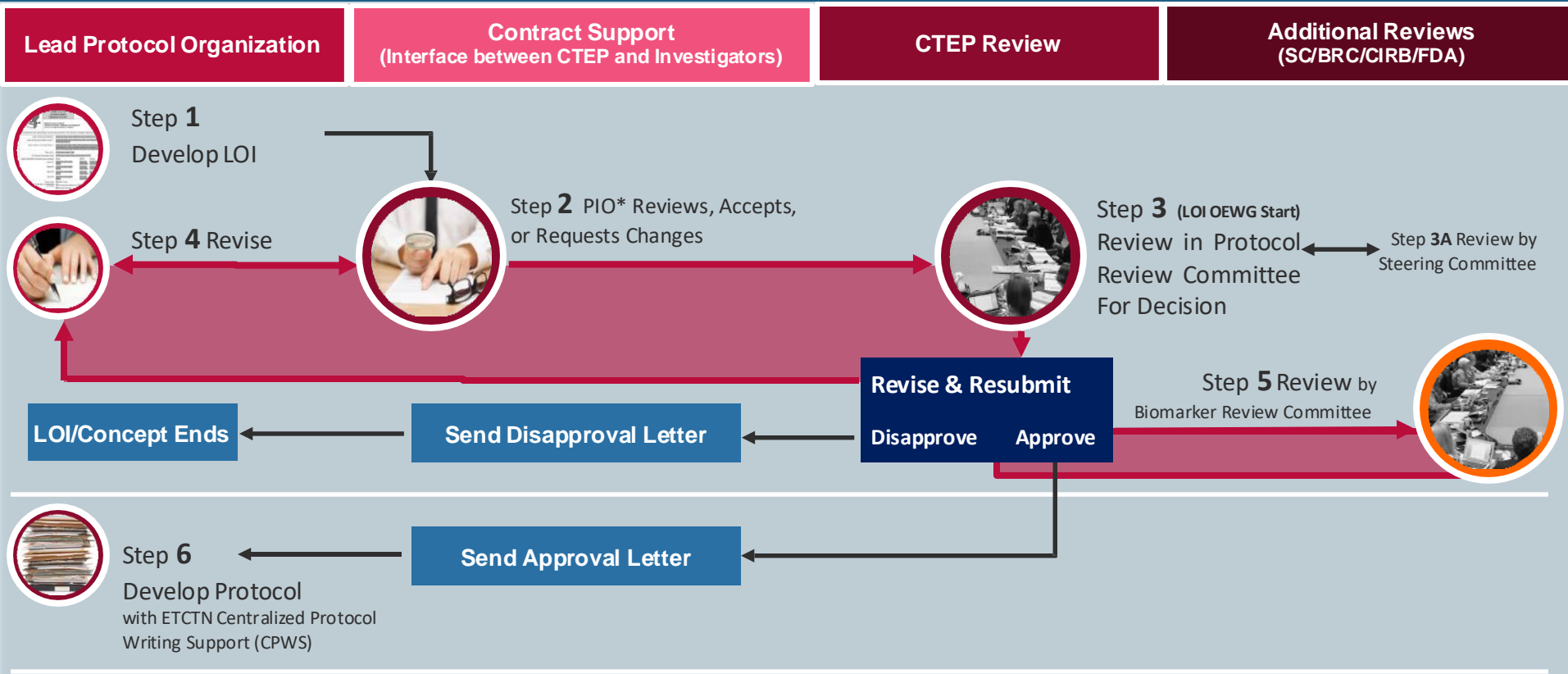
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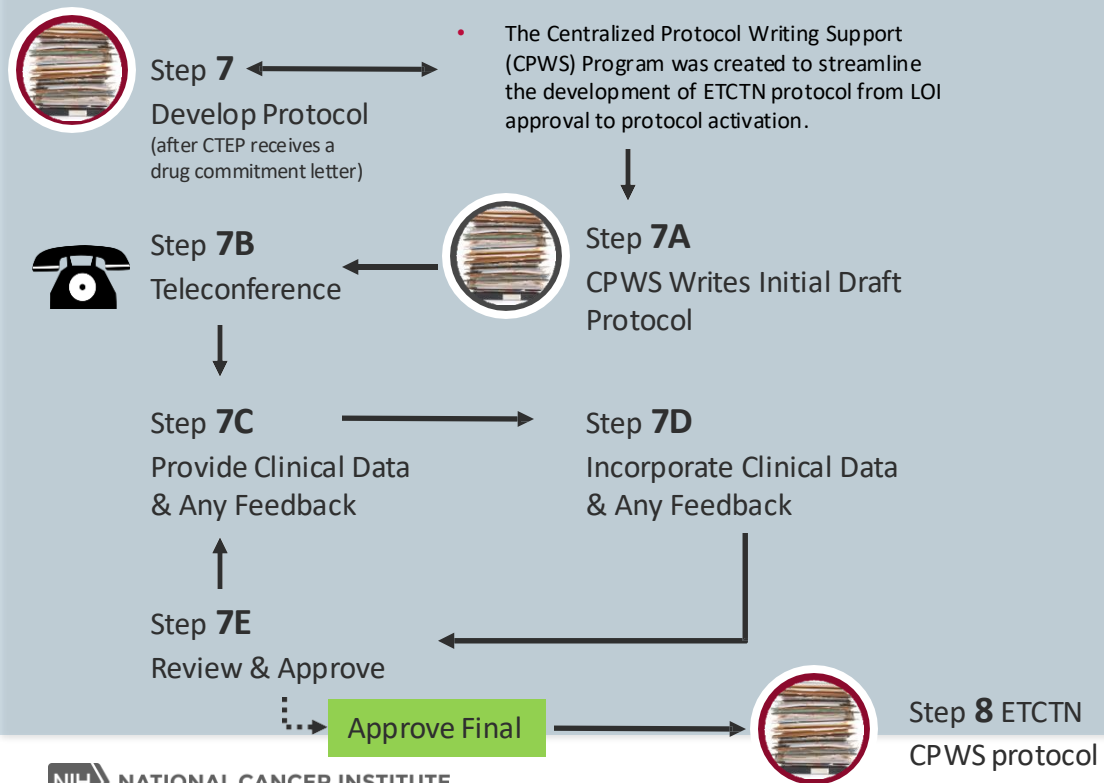
Projected Accrual Dates: [Click and enter Date] to [Click and enter Date]

CTEP: Document Workflows for ETCTN Letters of Intent (LOI)

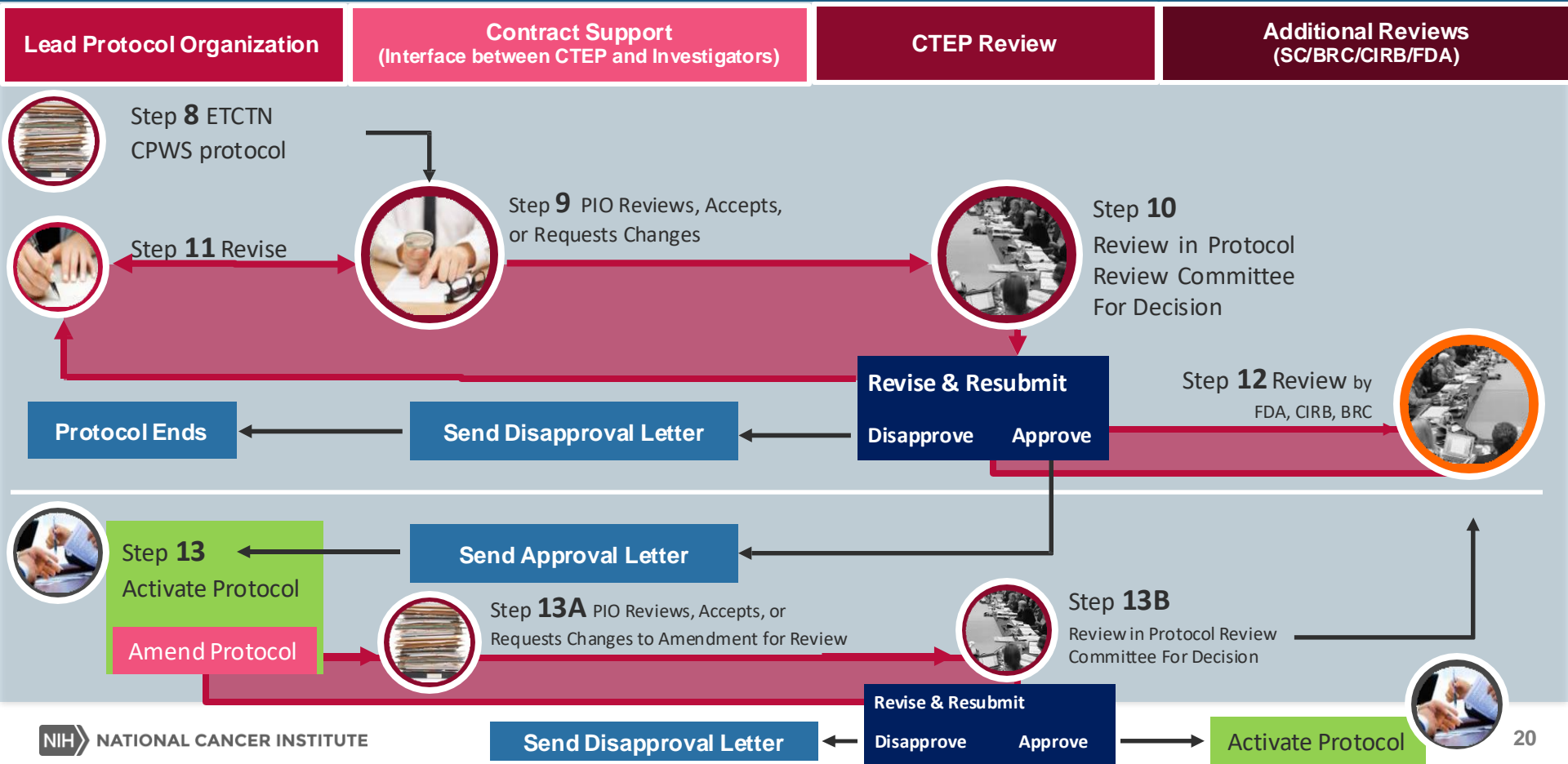


*PIO = CTEP Protocol Information Office

CTEP: Centralized Protocol Writing Support (CPWS) Program



CTEP: Document Workflows for Letters of Intent (LOI) or Concepts



- **Accrual**
 - Smaller patient populations to study arise due to molecularly-defined diseases
 - Need of a scalable/flexible program that can rapidly adapt to recruitment gaps
- **Biomarker-driven studies**
 - Tissue acquisition hurdles
 - Fit-for-purpose, validated assays
 - Functional imaging
- **Driving discovery to patients**
 - To and from bench to bedside collaborations
 - More predictive animal models to evaluate tumor heterogeneity



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