NCI-Academic-Industry Partnerships for Cancer Therapeutics Development

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I have no disclosures

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Optimizing Public-Private Partnerships for Clinical Cancer Research
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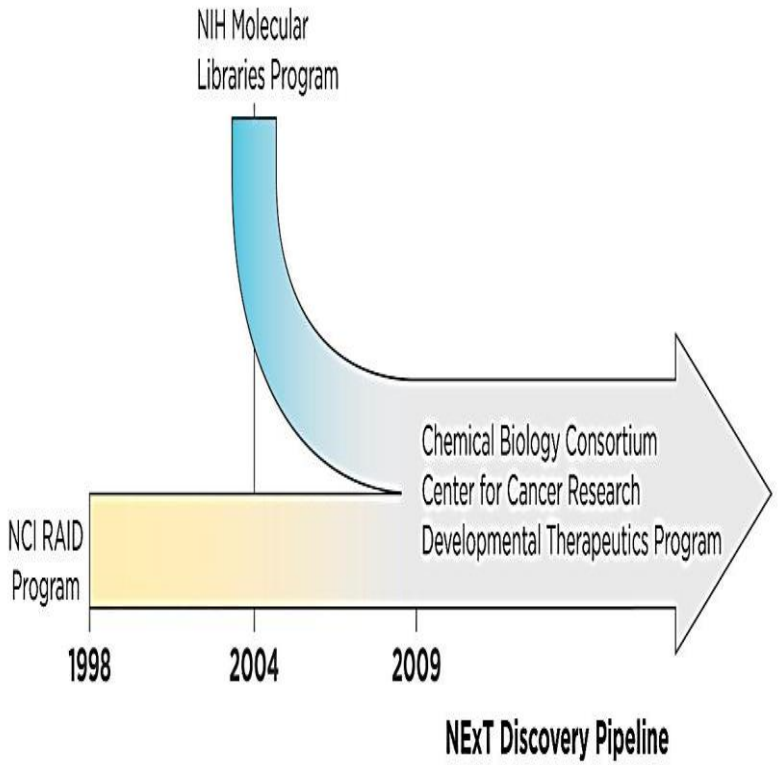
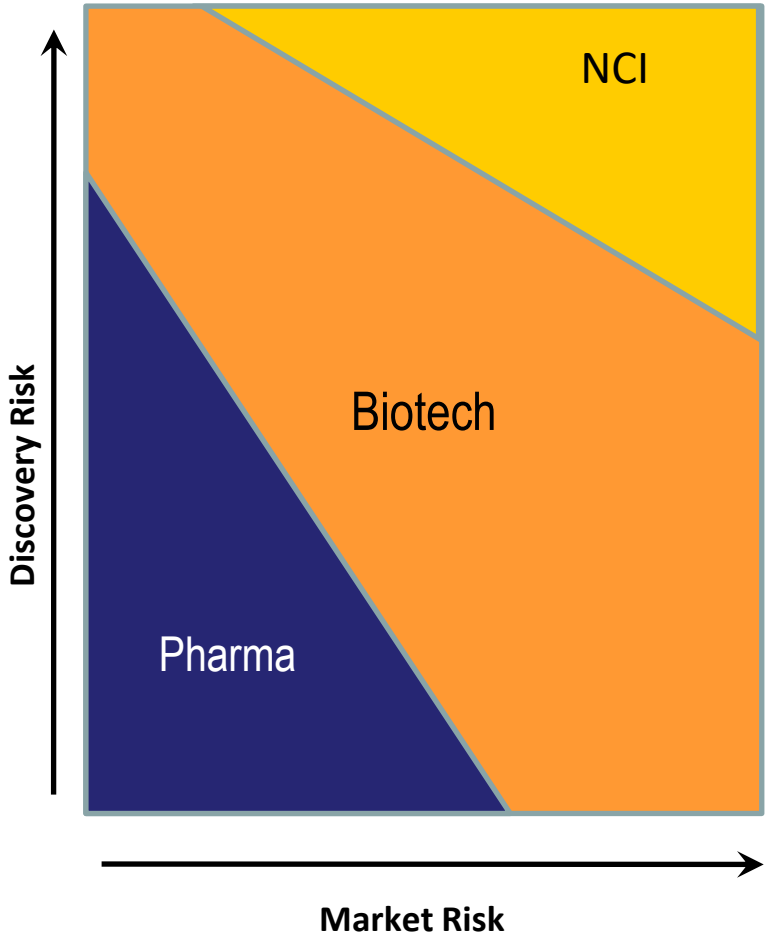
Overview

- NCI's Experimental Therapeutics (NExT) Pipeline: PPP for therapeutics development from drug discovery to phase I-II trials
- NCI Clinical Trials and PPP's by the numbers
- Exemplar: CIMAC-CIDC-PACT
- Pros and Cons of PPPs

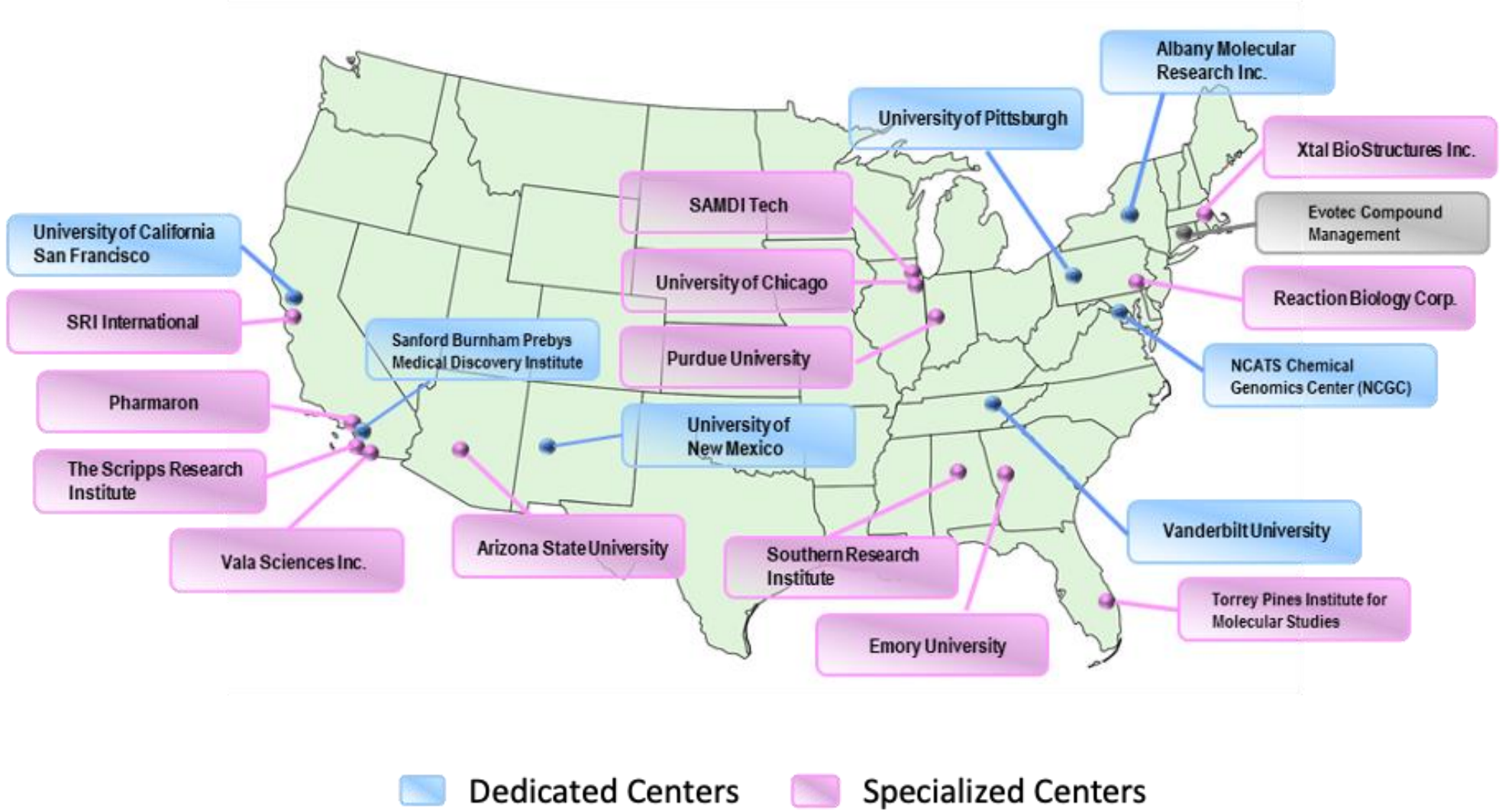
Origin and Goals of the NExT Discovery & Development Pipeline



- **NExT (NCI Experimental Therapeutics Program) builds on >60 yrs of NCI experience in cancer drug development to increase flow of early & late-stage candidates from Academia/small biotech/Pharma to the clinic**
- **CBC (Chemical Biology Consortium) is an integrated network of chemical biologists focusing on DRUG DISCOVERY**
- **DRUG DEVELOPMENT: Animal efficacy, PK, PD, Tox, & GMP scale up: Performed at FNLCR or by NCI contractors**
- **Not intended to replicate Pharma**
- **Not a grant program; provides access to drug development services**
- **Focus on developing therapies for underrepresented malignancies & on difficult targets; longer time horizon**
- **NCI committed to projects from <u>inception through proof-of-concept, PD-driven clinical trials</u>**



NCI Chemical Biology Consortium: Discovery Arm of NExT



NExT: From Application Review to Project Team Kickoff Meeting

Project Applications submitted to NExT
(3 cycles per year)

Projects range from HTS/target validation to Phase I/II Trials:
small molecules, biologics, imaging agents

Special Emphasis Panel
(SEP)

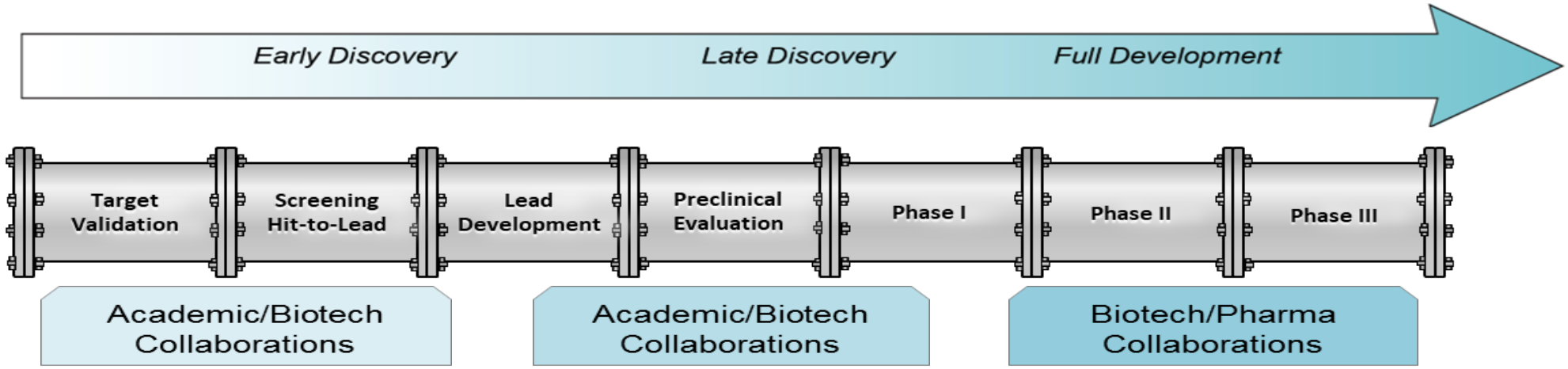
Highly ranked projects

- **ETCTN & NCTN: Ph 1 & 2 Trials**
- **Early-phase Project Teams**
- **Investigational Drug/Disease Steering Committee**
- [Grant Programs for Trials; FNLCR for PD]

CBC Steering Committee Endorsement
[Leidos/FNLCR Subcontracts]

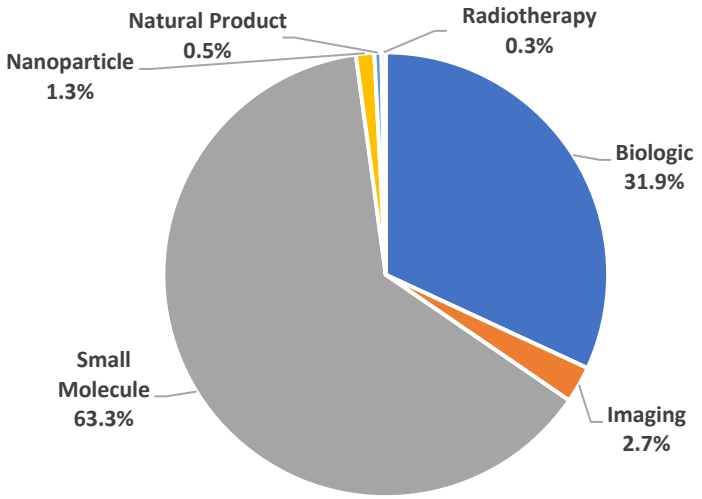
- **Project planning; RFP issued**
- **Selection of CBC Centers**
- **NCI approval of Resources**
- **Subcontracts managed by Leidos/FNLCR**
- **Project team kickoff meeting**

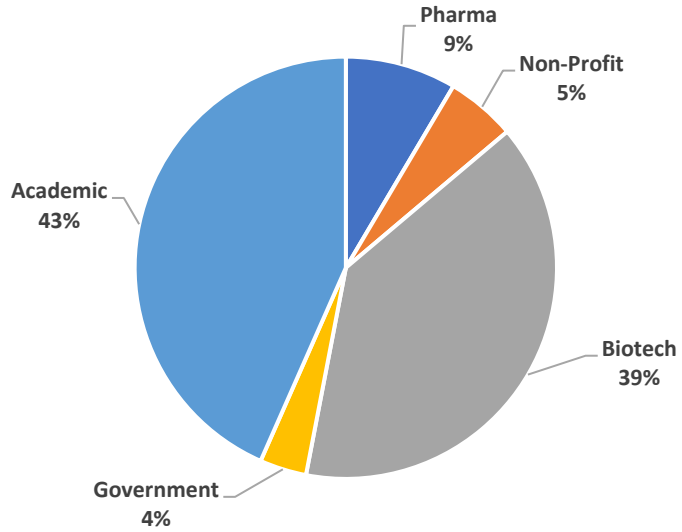
NExT Program Metrics: A Diversified Portfolio

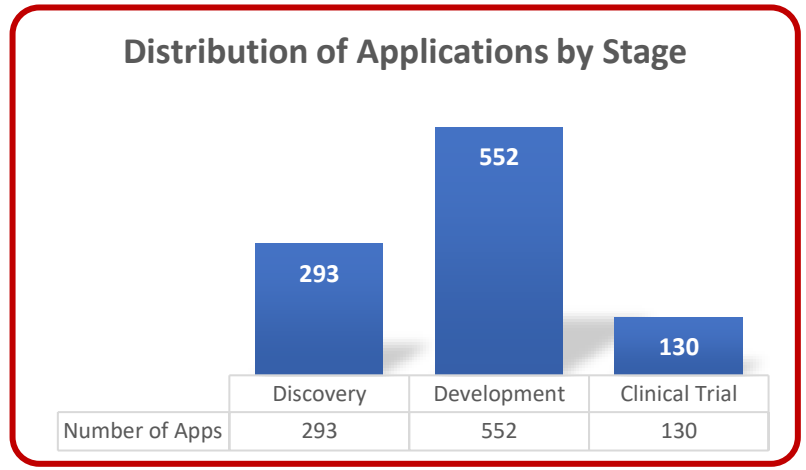


Projects enter the pipeline on a competitive basis at any stage of the pipeline

Since inception in 2009 NExT has received > 1100 applications: 10-14% success rate







DCTD/CTEP Overall Clinical Trials Portfolio

- Full spectrum of Clinical Trials (Phase 0, Phase 1, Phase 2, and Phase 3)
- Currently uses 129 investigational agents supported by 184 Investigational New Drug Applications (INDs) – CTEP/DCTD is the legal sponsor
- Approx. 20,000 registered investigators at over 2,000 institutions in the US and internationally
- Over 270 actively accruing clinical treatment trials
- About 59 new treatment trials opened per year; 72% CTEP held INDs
- Approx. 17,000-20,000 patients enrolled/year on treatment trials

Every Step in Trials Development Requires Agreements

- Confidential Disclosure Agreements (CDA's)
- Material Transfer Agreements (MTA's)
- Research Collaboration Agreements (RCAS's) (basically an MTA+CDA)
- Clinical Trials Agreement (CTA's) (an RCA with a clinical component)
- Cooperative Research and Development Agreements (CRADAs) (special agreement for government collaborations that allow outside funding and guarantee of IP rights)

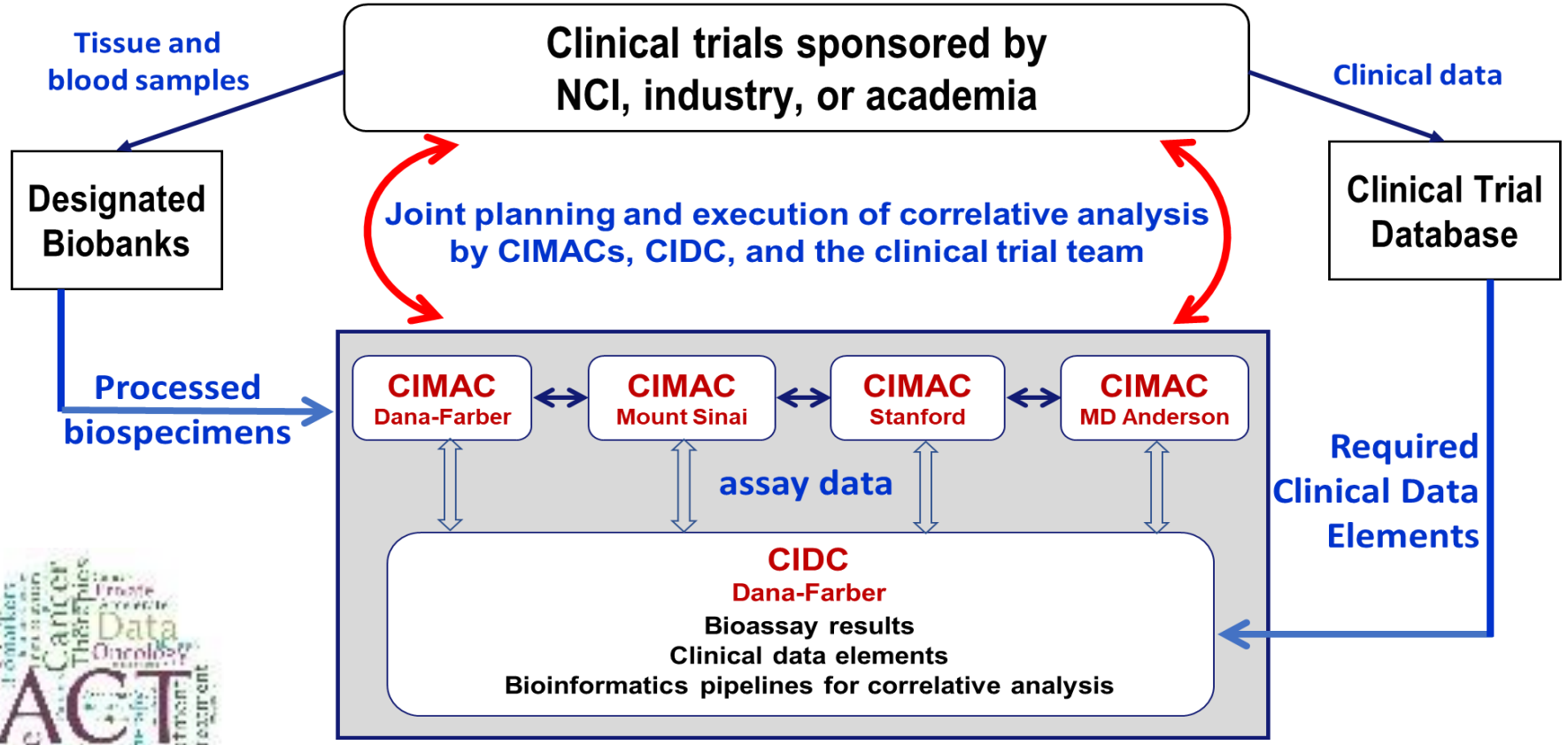
DCTD/CTEP Active Collaborators: A-J Only

AbbVie, Inc.	Biosplice Therapeutics	Faeth Therapeutics
Acrotech Biopharma, LLC	Blueprint Medicines	Genentech, Inc.
Actinium Pharma, Inc.	Boehringer Ingelheim	Gilead Sciences, Inc.
Agios, Pharmaceuticals	Bristol-Meyers Squibb	GlaxoSmithKline, LLC.
Alkermes, Inc.	Celldex	GlycoMimetics, Inc.
Amgen, Inc.	Celgene Corporation	Horizon Pharma
Aprea Therapeutics	Cleave Biosciences, Inc.	IGM Biosciences, Inc.
Ascentage Pharma Grp.	Cornerstone Pharma	Illumina, Inc.
Astellas Pharma, Inc.	Curis, Inc.	ImmunityBio
Astex Therapeutics, Ltd.	Cybrexa, Inc.	ImmunoGen, Inc.
AstraZeneca, Inc.	Eli Lilly and Co.	Ipsen Biopharma
Bayer HealthCare, Inc.	EMD Serono	Janssen R &D, LLC
Bellicum Pharma, Inc.	Epizyme, Inc.	Jazz Pharmaceuticals
Biomed Valley Disc., Inc.	Exelixis, Inc.	Johnson & Johnson, LLC

- >110 active corporate collaborators from Large Pharma, to Biotech of all sizes, & Diagnostics Co.'s including NGS providers
- 16 agreements with International Organizations
- 1000's of ancillary agreements pursuant to large scale collaborations (MTAs, RCAs, CTAs)
- 153 days average time from project approval to CRADA execution (6 mo drop dead date)
- Evolution from one drug one company to one umbrella trial, many companies

CIMAC-CIDC-PACT Network

[Cancer Immune Monitoring & Analysis Centers]
[Cancer Immunologic Data Center]
[Partnership for Accelerating Cancer Therapies]



- **35 IO trials**
- **>2000 pts**
- **1000's assay samples**
- **Assay validation & harmonization across network**
- **>150 publications**
- **Multiple disease and IO modalities**

$60 Million over 5 years from NCI (2017-2022)

Current PACT Partners

abbvie

AMGEN

Boehringer Ingelheim

Bristol-Myers Squibb

Celgene

Genentech
A Member of the Roche Group

GILEAD

gsk

janssen Oncology
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

NOVARTIS

Pfizer

SANOFI

Each partner committed $5 million over 5 years =

Total investment of $60 million/5 years

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FDA

FNIH
Foundation for the National Institutes of Health

PhRMA

- Joint governance procedures
- Enhance biomarker standardization
- Develop exploratory IO biomarkers & incorporate these into PACT clinical trials
- Enhance CIDC database for cross trial analyses

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PROS

- The NCI is uniquely situated to act as a neutral third party to facilitate interactions between organizations that normally have difficulty working together – e.g. NCI sponsors a large number of combination studies from 2 or more drug/diagnostic companies
- Strict timelines facilitate agreement negotiation (6 month ‘drop dead’)
- Agreements allow resource pooling so all parties can contribute resources to development
- Everyone knows the expectations and rights (IP, data sharing, publication) going into the negotiation

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CONS

- Rigid and non-flexible agreement terms can be challenging (terms cannot change because they must be consistent with pre-existing agreements); some partners do not want to participate under existing frameworks (government requirements)
- CRADA requirements, previously negotiated, may make interactions across NCI programs difficult
- High turnover amongst industry negotiation staff often requires ‘re-litigation’ of ‘settled’ issues; and business (rather than scientific) decisions not infrequently abnegate signed agreements
- May not be possible to provide the amount of oversight a partner desires; can lead to friction with partners who are used to having a greater degree of control over a project (pursued with a contractor, for example, rather than an academic or government partner)

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LESSONS LEARNED

- Trust but verify: Degree of clarity regarding roles, responsibilities, deliverables, and metrics directly proportional to the odds for success of the partnership—does everyone acknowledge the “rules of the road”? This includes ALL parties: Academic, Industry, and Government
- All parties must jointly believe in the strong scientific/clinical benefit of initiating the collaboration
- Never be surprised when/if a business decision overrides scientific rationale
- Whenever possible support the consistency of negotiating personnel and scientific ‘champions’
- A PPP that functions well requires a very high level of ‘care and feeding’