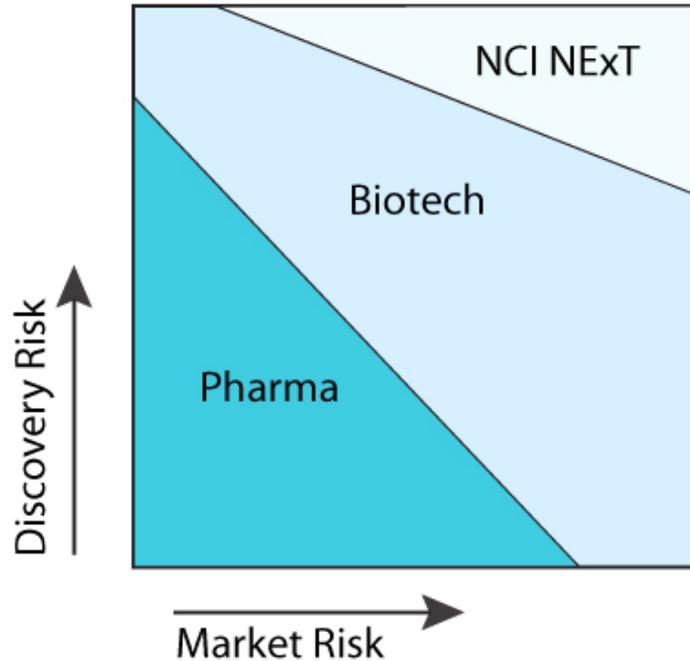# NCI Experimental Therapeutics Program Chemical Biology Consortium

James H. Doroshow, M.D.
Director, Division of Cancer Treatment and Diagnosis
National Cancer Institute, NIH

NIH ❯ **NATIONAL CANCER INSTITUTE**

Frederick National Laboratory
Advisory Committee
October 30, 2017
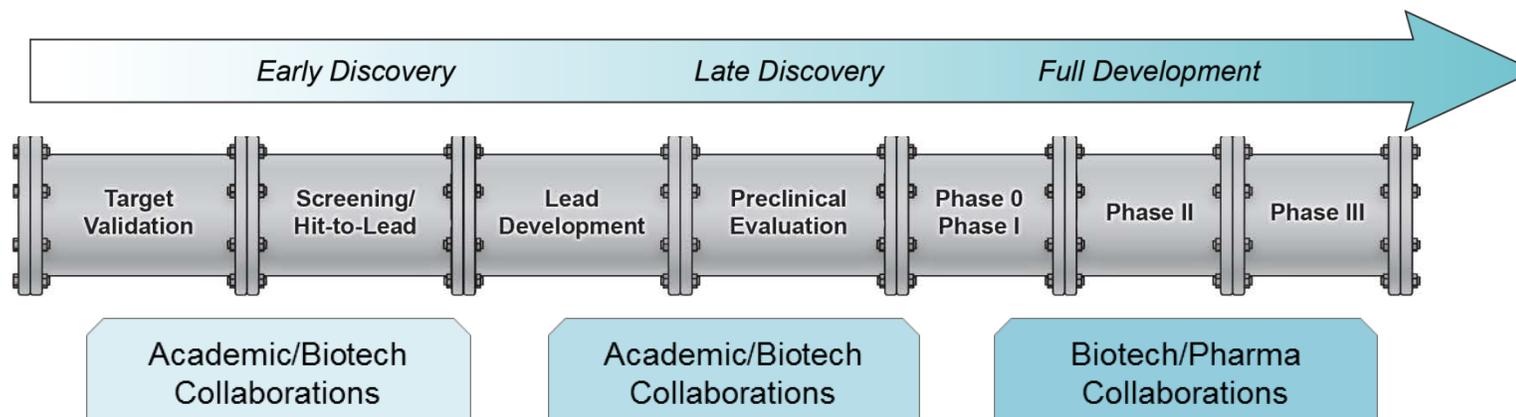
NCI's Experimental Therapeutics Program

Focus on indications NOT adequately addressed by the
pharmaceutical sector
and
recalcitrant, rare and neglected tumors

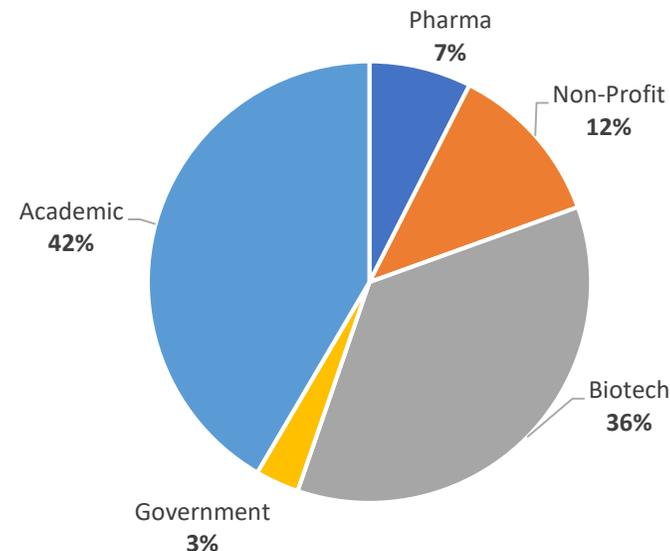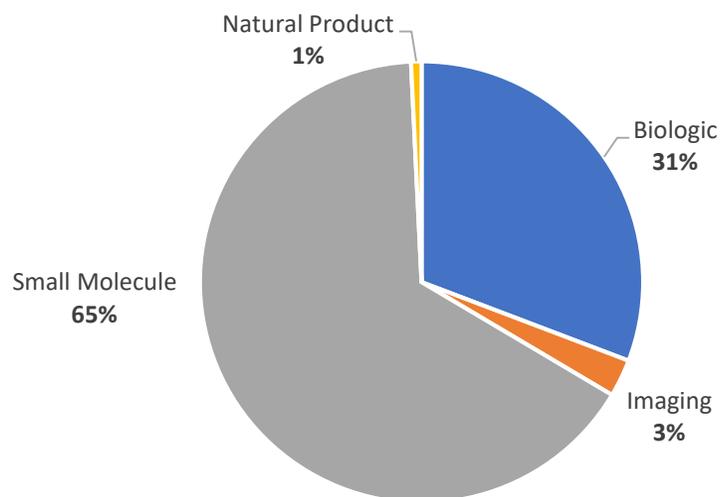**NExT is less risk-averse than Pharma**

NExT is *not a grant mechanism*; applications with exceptional science are not accepted without justification of a clinical application or potential benefit to patients.

NCI partners with applicants to facilitate milestone-driven progression of projects focused on discovery and development of novel therapeutics

NCI Experimental Therapeutics (NExT) Pipeline

Early Discovery — Late Discovery — Full Development

Target Validation | Screening/Hit-to-Lead | Lead Development | Preclinical Evaluation | Phase 0 Phase I | Phase II | Phase III

Academic/Biotech Collaborations | Academic/Biotech Collaborations | Biotech/Pharma Collaborations
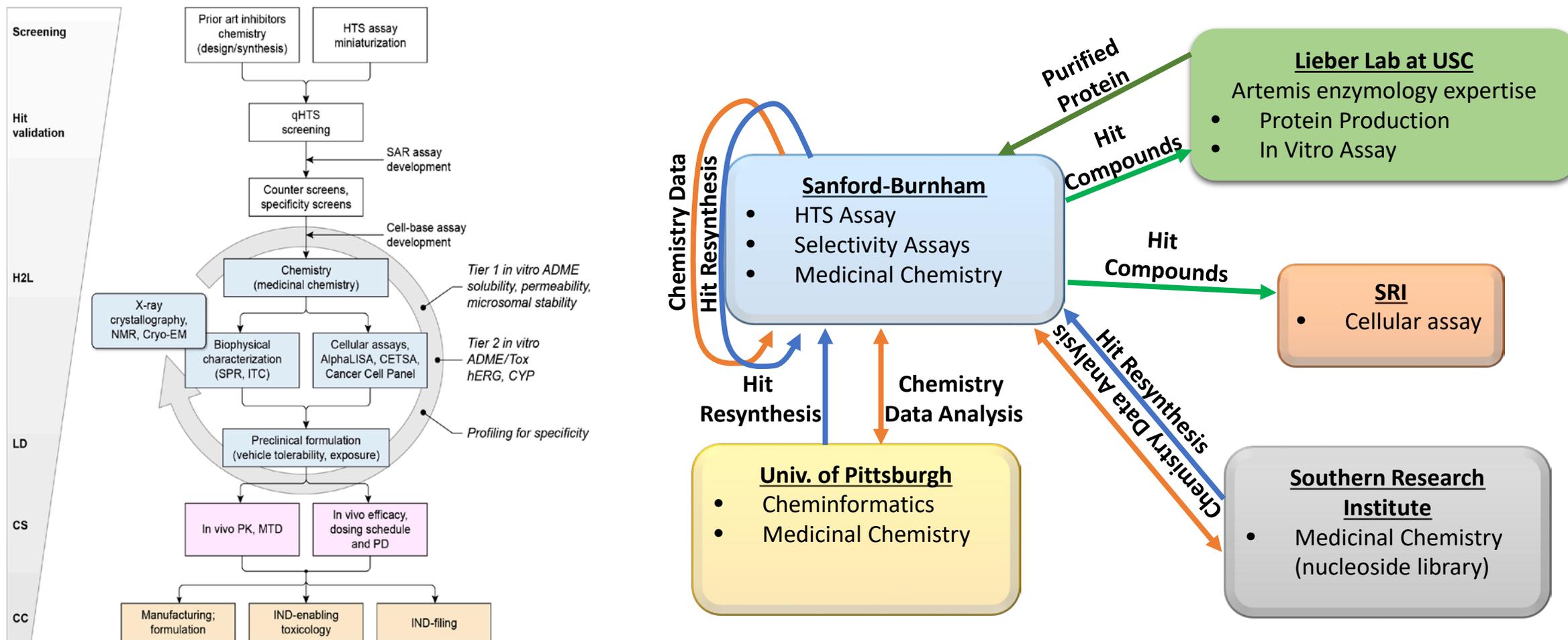
Projects enter the pipeline on a competitive basis at any stage of the pipeline
Since inception in 2009 NExT has received over 650 applications

Natural Product 1%
Biologic 31%
Small Molecule 65%
Imaging 3%

Pharma 7%
Non-Profit 12%
Academic 42%
Biotech 36%
Government 3%

Spring 2016: CBC Network Expanded to 23 Centers

University of Pittsburgh

Albany Molecular Research Inc.

Beryllium Discovery Corp.

Xtal BioStructures Inc.

Reaction Biology Corp.

NIH Chemical Genomics Center

University of North Carolina at Chapel Hill

Vanderbilt University

Emory University

Torrey Pines Institute for Molecular Studies

University of California, San Francisco

Evotec Compound Management

SRI International

Pharmaron

Sanford Burnham Prebys Medical Discovery Institute

The Scripps Research Institute

Vala Sciences Inc.

Arizona State University

SAMDI Tech

University of Chicago

Purdue University

University of New Mexico

Southern Research Institute

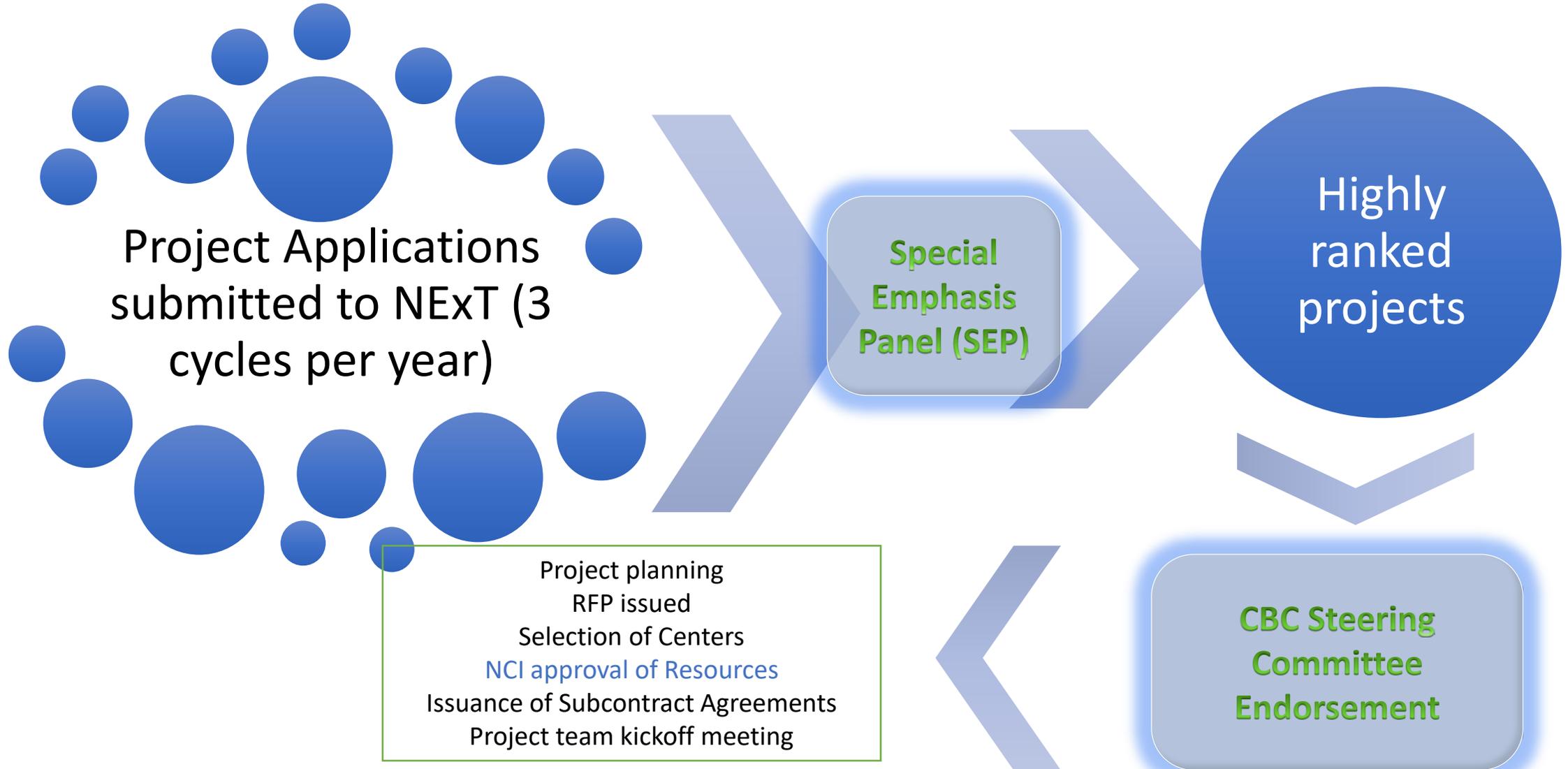Early Discovery → Late Discovery/Preclinical Evaluation
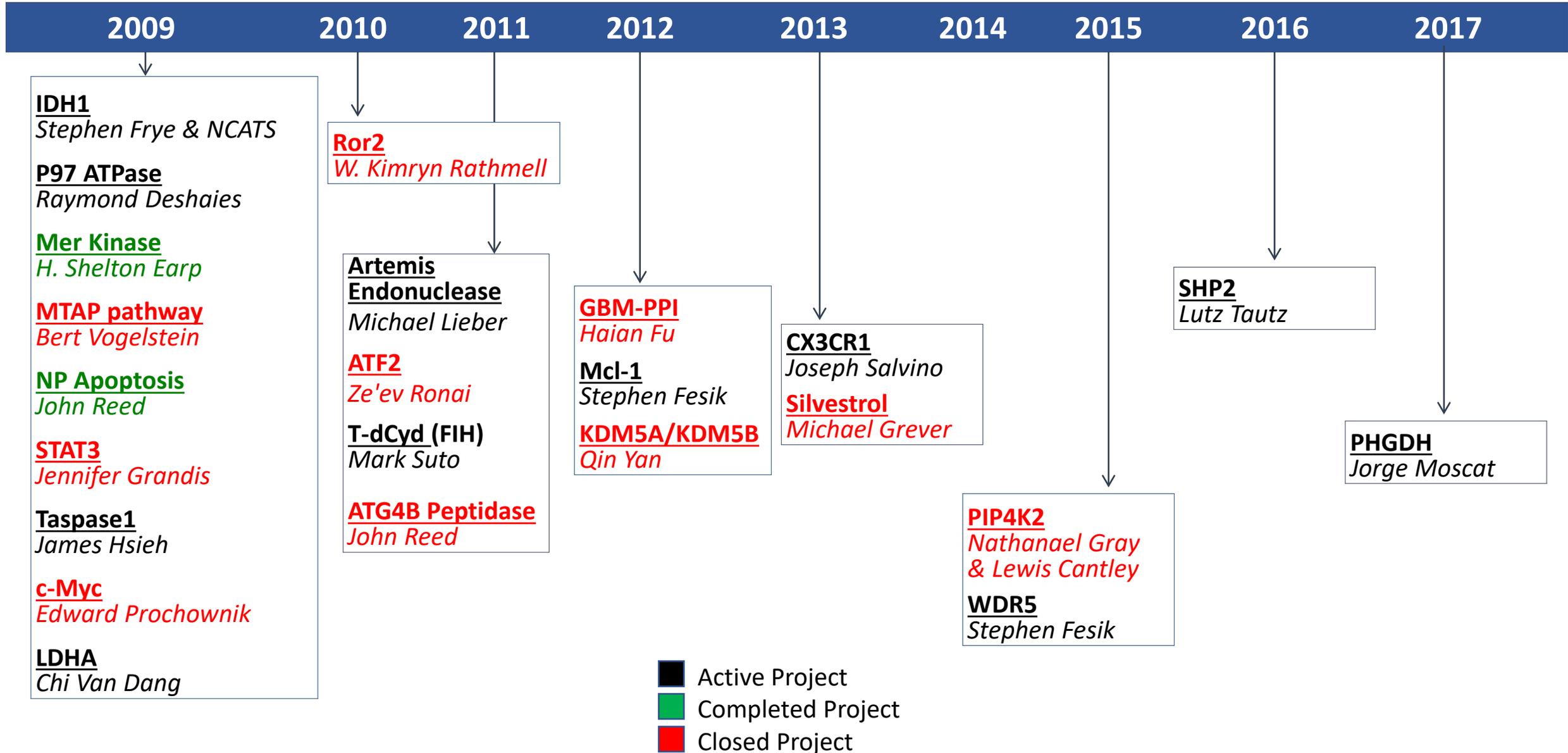
Team Science Approach to Fight Cancer

Breadth and Depth of Scientific Experience in Small Molecule Drug Discovery (CBC Centers) and Biology of Target (PI) is Highly valuable Asset in Project Progression to FIH Studies

Application Review to Project Team Kickoff Meeting

Project Applications submitted to NExT (3 cycles per year)

Special Emphasis Panel (SEP)

Highly ranked projects

CBC Steering Committee Endorsement

Project planning
RFP issued
Selection of Centers
NCI approval of Resources
Issuance of Subcontract Agreements
Project team kickoff meeting

(Participation on discovery projects is approved and funded by NCI and managed through subcontracts administered by Leidos Biomed)

Actively Managed Discovery Portfolio

2009 **2010** **2011** **2012** **2013** **2014** **2015** **2016** **2017**

IDH1
Stephen Frye & NCATS

P97 ATPase
Raymond Deshaies

Mer Kinase
H. Shelton Earp

MTAP pathway
Bert Vogelstein

NP Apoptosis
John Reed

STAT3
Jennifer Grandis

Taspase1
James Hsieh

c-Myc
Edward Prochownik

LDHA
Chi Van Dang

Ror2
W. Kimryn Rathmell

Artemis Endonuclease
Michael Lieber

ATF2
Ze'ev Ronai

T-dCyd (FIH)
Mark Suto

ATG4B Peptidase
John Reed

GBM-PPI
Haian Fu

Mcl-1
Stephen Fesik

KDM5A/KDM5B
Qin Yan

CX3CR1
Joseph Salvino

Silvestrol
Michael Grever

PIP4K2
Nathanael Gray & Lewis Cantley

WDR5
Stephen Fesik

SHP2
Lutz Tautz

PHGDH
Jorge Moscat

Active Project
Completed Project
Closed Project

SEP Voting and Ranking of Projects
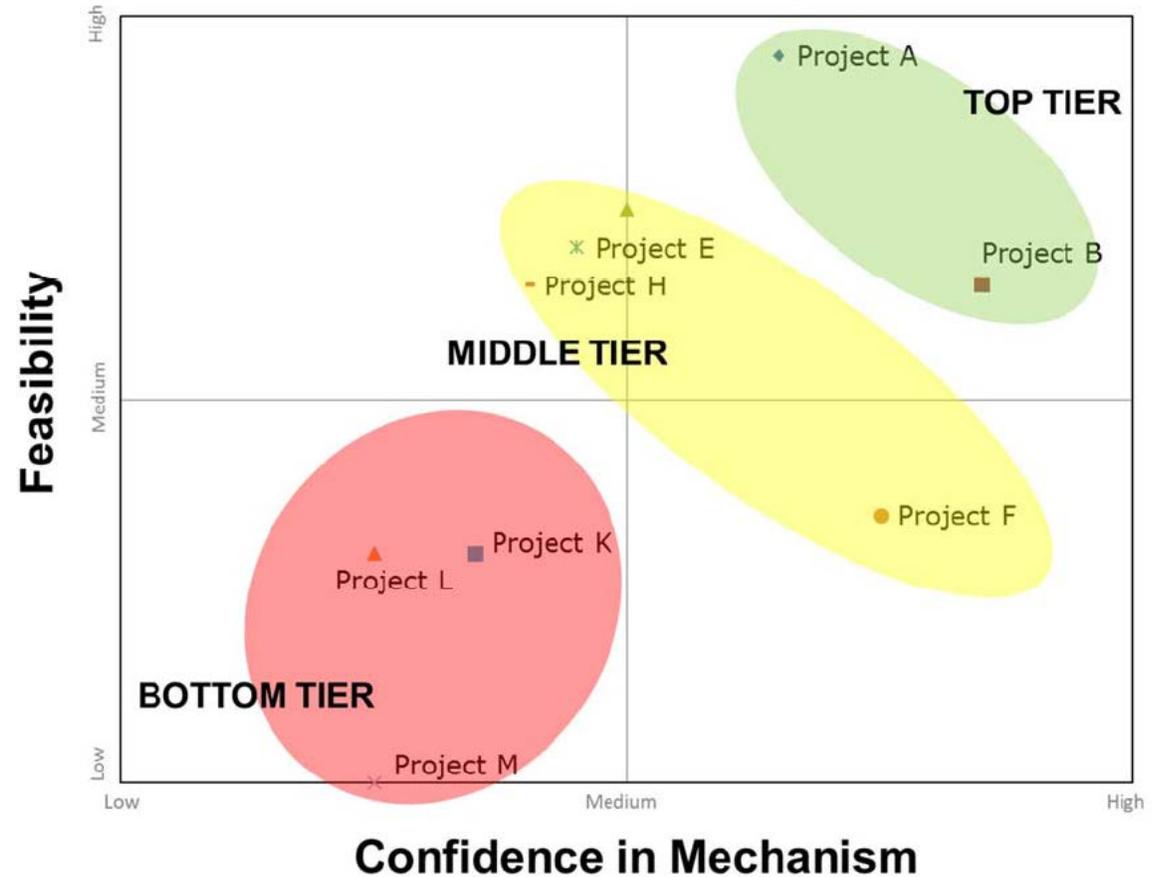
2017 CBC Portfolio Evaluation
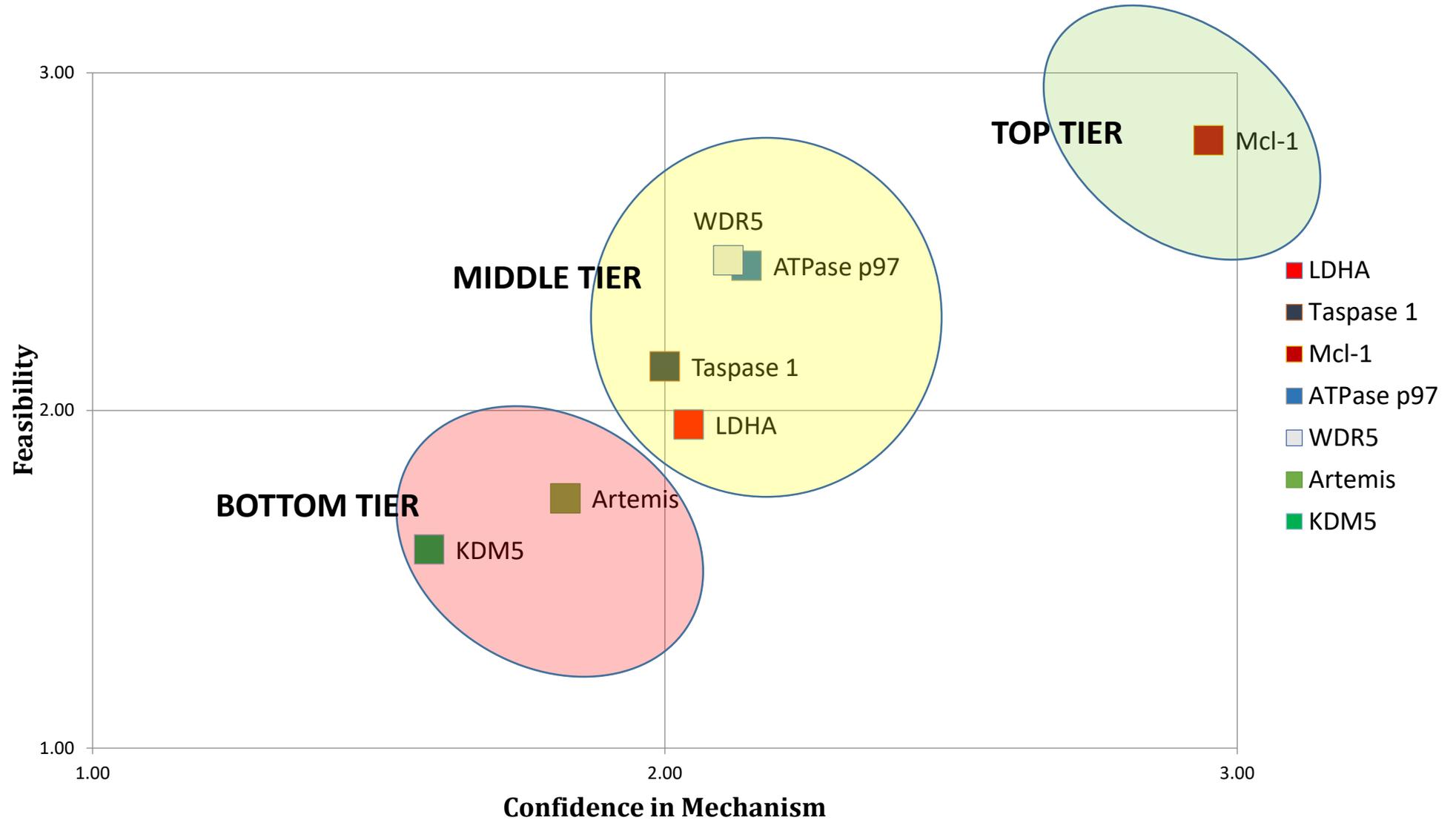
CBC Project Rankings: 2016 vs 2017