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

Since inception in 2009 NExT has received over 650 applications
Spring 2016: CBC Network Expanded to 23 Centers

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
Project Applications submitted to NExT (3 cycles per year)

Highly ranked projects

Special Emphasis Panel (SEP)

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
- 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
  
2010
- IDH1
  Stephen Frye & NCATS
- P97 ATPase
  Raymond Deshaies
- MTAP pathway
  Bert Vogelstein
- 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
  
2011
- 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
- SHP2
  Lutz Tautz
- PHGDH
  Jorge Moscat
- PIP4K2
  Nathanael Gray & Lewis Cantley
- WDR5
  Stephen Fesik

Legend:
- Black: Active Project
- Green: Completed Project
- Red: Closed Project
Mutant IDH1 inhibitor
AAA ATPase p97 inhibitor
Taspase1 inhibitor
WDR5-MLL1 inhibitor
LDHA inhibitor

Artemis Endonuclease inhibitor

Mutant IDH1 inhibitor
Mcl1 inhibitor

DNMT1 Inhibitors
Imaging agents:
NIR Fluorophore
EGFR Panitumumab
LUM015
SEP Voting and Ranking of Projects

NExT Portfolio Review Example

Project A

1. Feasibility
   - Low
   - Medium
   - High

2. Confidence in Mechanism
   - Low
   - Medium
   - High

3. Additional Comments

Feasibility vs. Confidence in Mechanism Diagram:
- **TOP TIER**
  - Project A
  - Project B

- **MIDDLE TIER**
  - Project E
  - Project H

- **BOTTOM TIER**
  - Project I
  - Project K
  - Project M
  - Project F
2017 CBC Portfolio Evaluation

Feasibility vs Confidence in Mechanism

- TOP TIER: Mcl-1
- MIDDLE TIER: WDR5, ATPase p97, Taspase 1
- BOTTOM TIER: LDHA, Artemis, KDM5
CBC Project Rankings: 2016 vs 2017

2016

2017