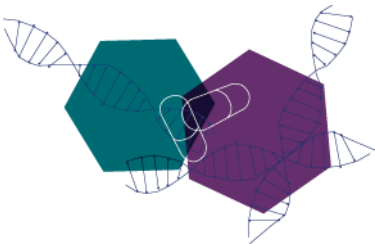
Catalyzing Innovation: NIH National Center for Advancing Translational Sciences

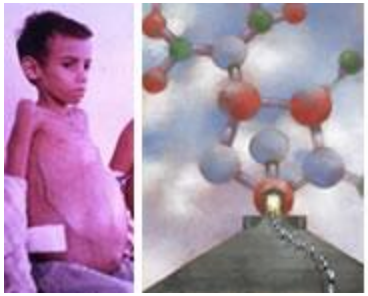
Lili M. Portilla, MPA
Director, Office of Strategic Alliances
National Center for Advancing Translational Sciences (NCATS), NIH
Email: Lili.Portilla@nih.gov

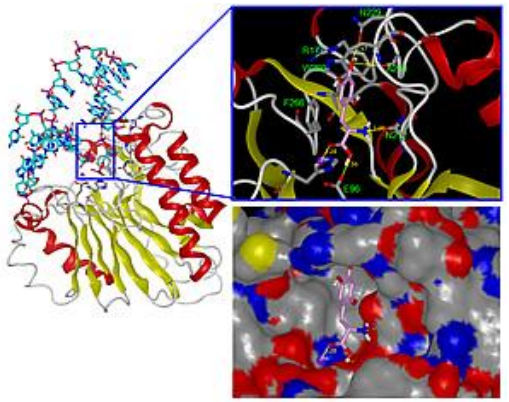
NIH National Center for Advancing Translational Sciences



Division of Pre-Clinical Innovation (DPI)

- Therapeutics for Rare and Neglected Diseases (TRND)
- Toxicology in the 21st Century (Tox21)
- Bridging Interventional Development Gaps (BrIDGs)
- Molecular Libraries Probe Production Center
- Assay Development





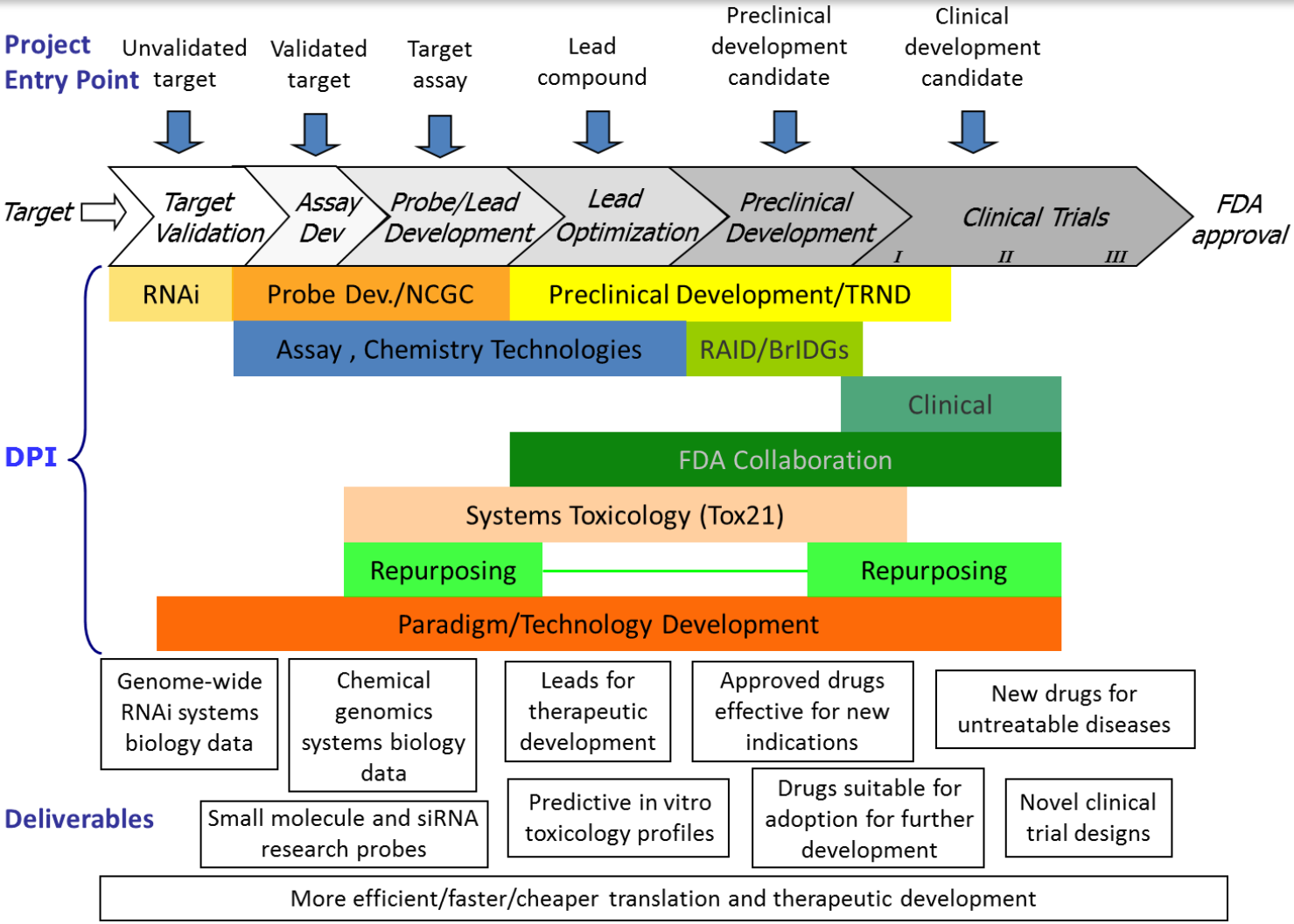
DPI currently has 300+ collaborations with investigators across the U.S. and around the world.

NIH National Center for Advancing Translational Sciences

DPI is Different in Science and Operation

- DPI is administratively intramural
  - No independent PIs, **no tenure** system; 80% of staff ex-industry
  - All projects are **collaborations,** 90% of which are with extramural investigators/foundations/companies
  - Projects are selected via **solicitation/review**
- Science is intermediary between mechanistic research and commercialization
  - Each project has **tangible deliverable** and technology/paradigm development components
- It is **disease agnostic,** works across disease spectrum
  - **Common mechanisms** and principles to make translation better/faster/cheaper for all
- Focuses on **new technologies, enabling tools, dissemination**

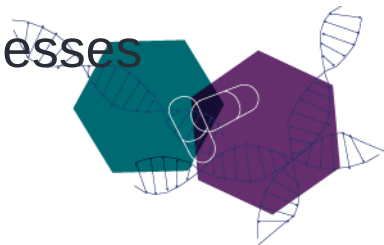
NCATS DPI: A Collaborative Pipeline



National Center for Advancing Translational Sciences

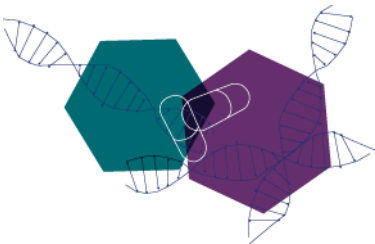
Bridging Interventional Development Gaps (BrIDGs) Program

- Model: Contract access collaboration between DPI and extramural labs (Formerly NIH-RAID Program)
- Projects
  - Enter with clinical candidate identified
  - Any disease eligible
  - Gap analysis followed by data generation using DPI contracts to generate data necessary for IND filing
  - Exit at or before IND
  - Milestone driven
  - Therapeutic modalities: any (small molecules, peptides, oligonucleotides, gene therapy, antibodies, recombinant proteins)
- Eligible Applicants
  - Academic (US and Ex-US), Non-Profit, SBIR eligible businesses



BrIDGs Highlights

- 180 applications submitted since 2005
  - 34 approved
- 19 completed projects (two in FY12)
  - 12/12 submitted INDs approved
  - 5 projects in Phase 1, three in Phase II
  - 5 agents licensed during or after BrIDGs involvement



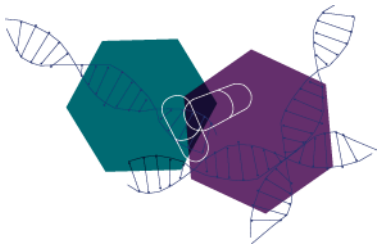
BrIDGs Portfolio

Applicant	Organization Name	Org Type	Agent	Disease	Funding
Au, Jessie	Optimum Therapeutics	Biotech	Small Molecule	Pancreatic Cancer	Common Fund
Bankiewicz, Krystof	University of California San Francisco	Academic	Gene Vector	Aromatic L-amino acid decarboxylase	CF/NINDS
Bloch, Kenneth	Massachusetts General Hospital	Academic	Small Molecule	FOP & Anemia of Inflammation	CF/NIAMS/NIDDK
Darling, Thomas	Edunn Biotechnology	Biotech	Oligonucleotide	Alzheimer's disease	CF/NIA
De Leon, Diva	Children's Hospital of Philadelphia	Academic	Peptide	Hyperinsulinism	Common Fund
Donn, Karl	Parion Sciences, inc.	Biotech	Small Molecule	Chronic dry eye	Common Fund
Dowling, Peter	University of Medicine and Dentistry of New Jersey	Academic	Peptide	Multiple sclerosis	Common Fund
Evans, Christopher	Beth Israel Deaconess Medical Center	Academic*	Gene Vector	Osteoarthritis	Common Fund
Kunos, George	NIH/NIAAA	Intramural*	Small molecule	Metabolic syndrome	Common Fund
Mannstadt, Michael	Massachusetts General Hospital	Academic*	Peptide	Hypoparathyroidism	Common Fund
Mellon, Synthia	University of California San Francisco	Academic	Small Molecule	Niemann-Pick C	CF/NINDS
Miller, Kenneth	Kemmx Corporation	Biotech	Small molecule	Rheumatoid arthritis	CF/NIAMS
Rogawski, Michael	University of California, Davis	Academic*	Small molecule	Epilepsy	CF/NINDS
Sutula, Thomas	University of Wisconsin Madison	Academic*	Small Molecule	Epilepsy	Common Fund
Turner, Scott	Kinemed, Inc.	Biotech	Peptide	Atherosclerosis	Common Fund

* indicates that the investigator is partnered with a company

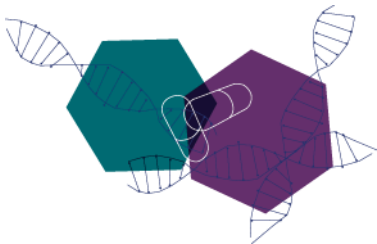
Therapeutics for Rare and Neglected Diseases (TRND) Program

- Model: Comprehensive drug development collaboration between DPI and extramural labs with disease-area / target expertise
- Projects
  - May enter at various stages of preclinical development
  - Disease must meet FDA orphan or WHO neglected tropical disease criteria
  - Taken to stage needed to attract external organization to adopt to complete clinical development/registration, max 2a
  - Milestone driven
  - Therapeutic modalities: small molecules, proteins
  - Serve to develop new generally applicable platform technologies and paradigms
- Eligible Applicants
  - Academic, Nonprofit, Government Lab, Biotech / Pharma
  - Ex-U.S. applicants accepted



TRND Highlights

- **14 projects through pilot phase & 2 public solicitations since 2009**
  - Mix of small molecules and biologics
  - Two innovative platform technologies
- **3 investigational drugs taken into humans**
  - CLL: IND filed with US FDA 7/12/11, approved 8/5/11
    - Phase I trial commenced 9/11
  - SCD: IND filed 10/14/11, approved 11/10/11
    - Phase I trial commenced 12/11
  - HIBM: Complete response filed 7/27/12, approved 8/24/12
    - Phase 1 trial in patients commenced 9/13/12
- **Initiated first natural history study**
  - HIBM: NIH Clinical Center, 1st patient enrolled September 2011
- **Every project is a unique Public-Private partnership**
  - Many include foundation and patient advocacy input



TRND Portfolio

Collaborator	Organization Name(s)	Partner Type(s)	Agent	Therapeutic Area / Disease
TRND Pilot Project	NPC-SOAR, Washington Univ., Einstein College of Medicine, NICHD, NHGRI	Disease Foundation, Academic, DIR	Repurposed Approved Drug	Niemann-Pick C
TRND Pilot Project	New Zealand Pharmaceuticals, NHGRI	Biotech, DIR	Intermediate Replacement	Hereditary Inclusion Body Myopathy
TRND Pilot Project	Aes-Rx, NHLBI	Biotech, DIR	NME	Sickle Cell Disease
TRND Pilot Project	Leukemia & Lymphoma Society, Kansas Univ. Cancer Center	Disease Foundation, Academic	Repurposed Approved Drug	Chronic Lymphocytic Leukemia
Reeves, Erica	ReveraGen BioPharma	Small Business	NME	Duchenne Muscular Dystrophy
Campbell, David	Afraxis, Inc.	Small Business	NME	Fragile X Syndrome
Garvey, Edward	Viamet Pharmaceuticals, Inc.	Small Business	NME	Cryptococcal Meningitis
Liu, Paul	NHGRI	DIR	Repurposed Approved Drug	Core Binding Factor Leukemia
Kimberlin, David	University of Alabama	Academic	Nucleotide Analog Pro-drug	Neonatal Herpes Simplex
Trapnell, Bruce	Cincinnati Children's Hospital	Academic	Biologic	Autoimmune Pulmonary Alveolar Proteinosis
Bloch, Kenneth	Massachusetts General Hospital	Academic	NME	Fibrodysplasia Ossificans Progressiva
Liu, Julie	CoNCERT Pharmaceuticals	Small Business	NME	Schistosomiasis
Davis, Robert	Lumos Pharma	Small Business	NME	Creatine Transporter Defect
Sazani, Peter	AVI BioPharma, Inc.	Small Business	Oligo (PMO)	Duchenne Muscular Dystrophy

Comparison of BrIDGs and TRND

BrIDGs	TRND
Contract Resource	Team-based Collaboration
PI must have identified lead agent	PI may start with lead optimized
No clinical trial support provided	Some clinical trial support provided
IP retained by owner	TRND may generate IP
Universal disease scope	Rare and neglected diseases only
Investigator prepares IND	Regulatory affairs assistance provided

Learn More About NCATS

ncats.nih.gov

- **Questions:** info@ncats.nih.gov
- **Like us on Facebook:** facebook.com/ncats.nih.gov
- **Follow us on Twitter:** twitter.com/ncats_nih_gov
- **Join our listserv, and subscribe to our e-newsletter via links at:** www.ncats.nih.gov/news-and-events/e-news/e-news.html