

# The NCATS' Rare Diseases Clinical Research Network (RDCRN) Program

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SESSION 7

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NCATS

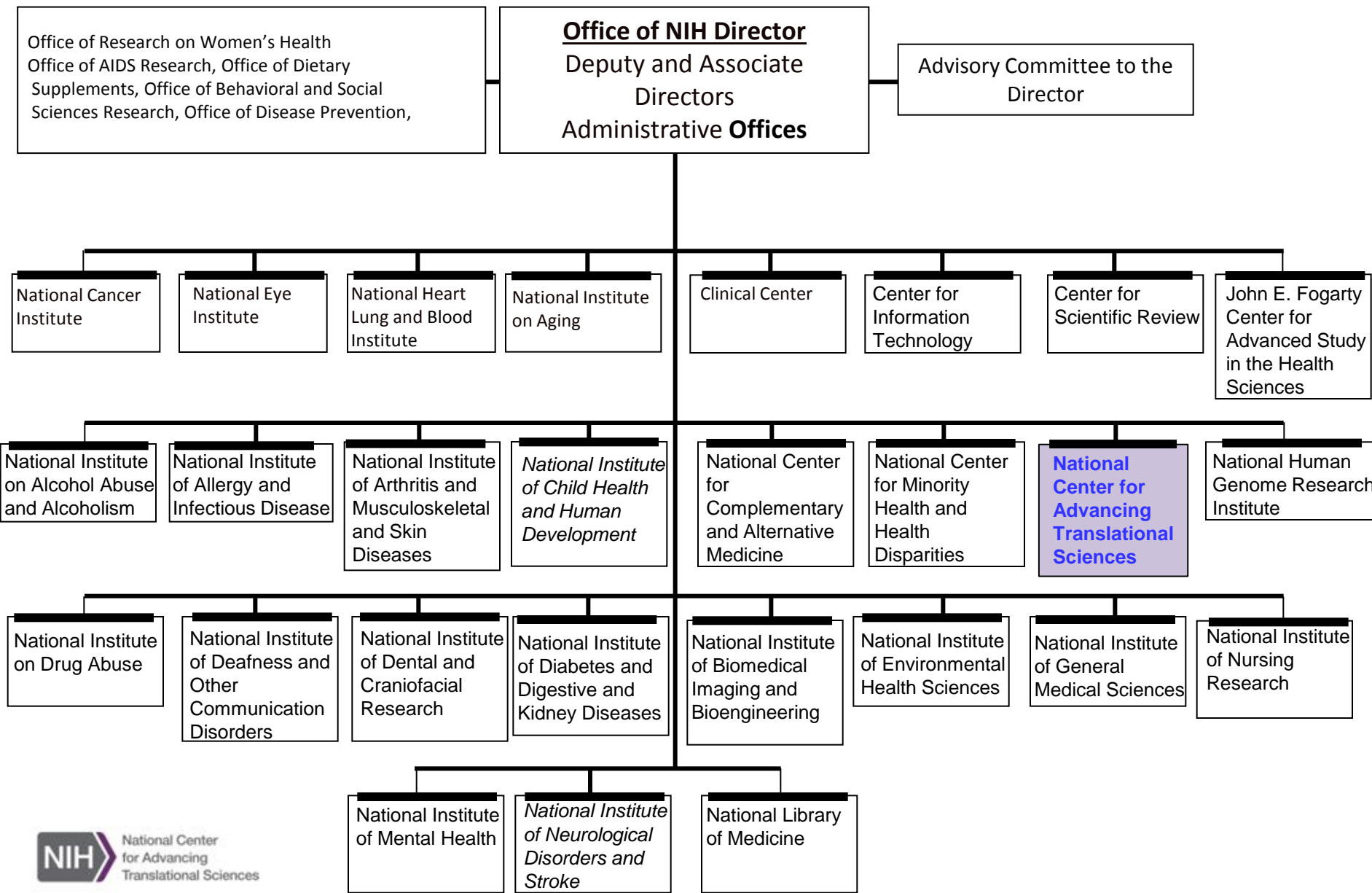
# *Rare Diseases Clinical Research Network (RDCRN) Program :*

A Model for Collaboration with Patients and  
Advocacy Groups to Facilitate Research  
Efforts

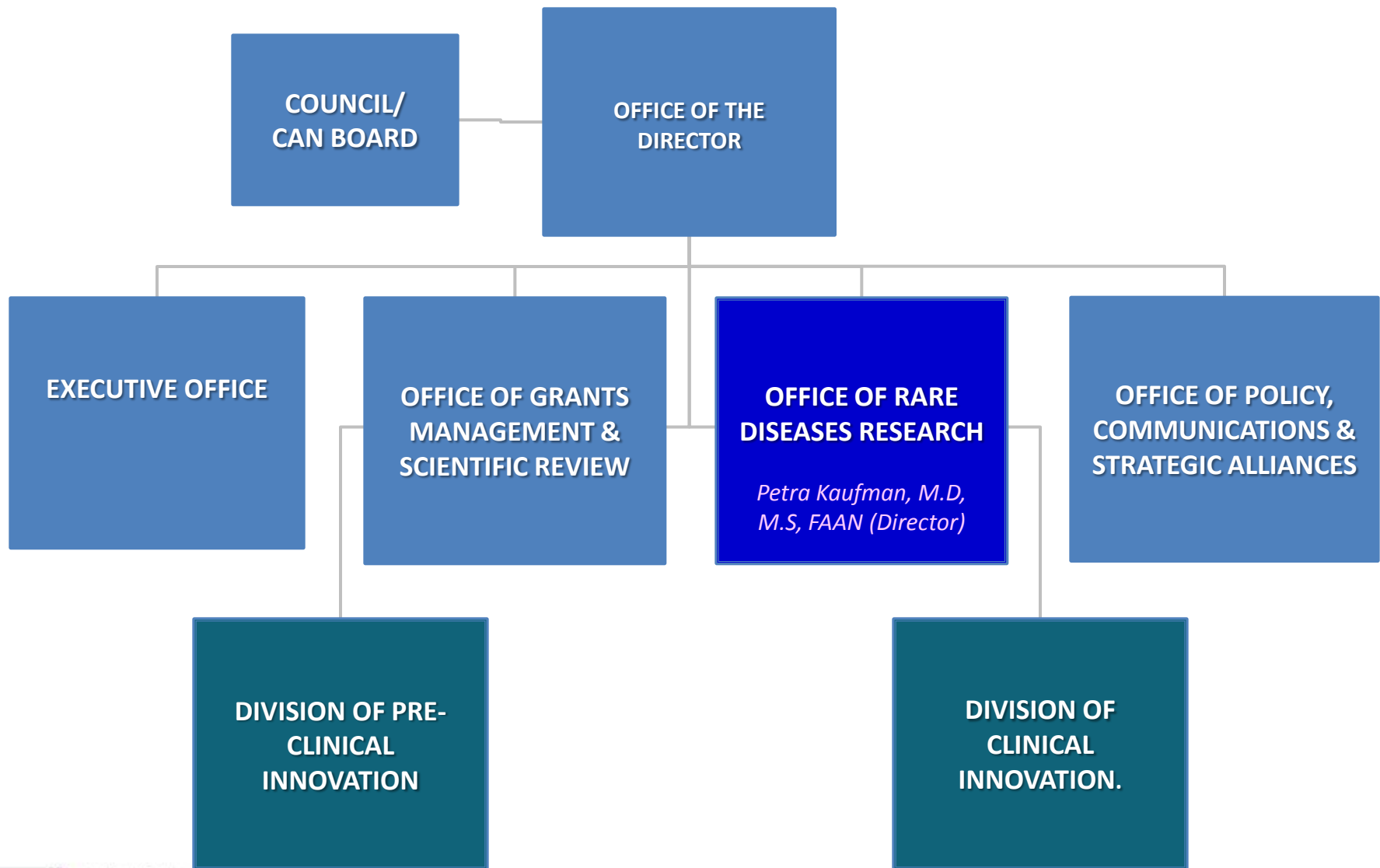
# Outline of talk

- RDCRN Program at ORDR, NCATS
  - Background
  - Goals
  - Collaborative partners
  - Special features of the program
  - Global partnership
  - Examples of successful collaborative efforts with patient advocacy groups

# A View of the National Institutes of Health (NIH), USA



# National Center for Advancing Translational Sciences (NCATS)



# Office of Rare Diseases Research (ORDR), NCATS Collaborative Programs/Initiatives

*Stimulates and coordinates research on rare diseases*

- **Rare Diseases Clinical Research Network (RDCRN) Program**
- Genetic and Rare Diseases Information Center (GARD)
- Scientific Conferences
- Global Rare Diseases Registry and Repository (GRDR)

# Rare Diseases: Background

- Prevalence < 200,000 people in the USA
- ~ 7000 Genetic and Acquired Rare Diseases
- Estimated 6%-8% of Population has a Rare Disease
- ~ 25 million people in the United States are affected

# Challenges for Rare Diseases Research

- Disease often not well characterized or defined
- Rarity means:
  - Recruitment for trials is usually quite difficult
  - Study populations become widely dispersed
  - Few expert centers for diagnosis, management, and research
- Often little high-quality evidence available to guide treatment



# RDCRN Program: Established by the Office of Rare Diseases Research (ORDR)



# RDCRN Program: Objective

The overall objective of RDCRN is to contribute to the clinical research and treatment for rare diseases by

- working collaboratively to identify biomarkers for disease risk, disease severity and activity, and clinical outcome
- while encouraging the development of new approaches to diagnosis, prevention, and treatment.

*PAGs as Research Partners*

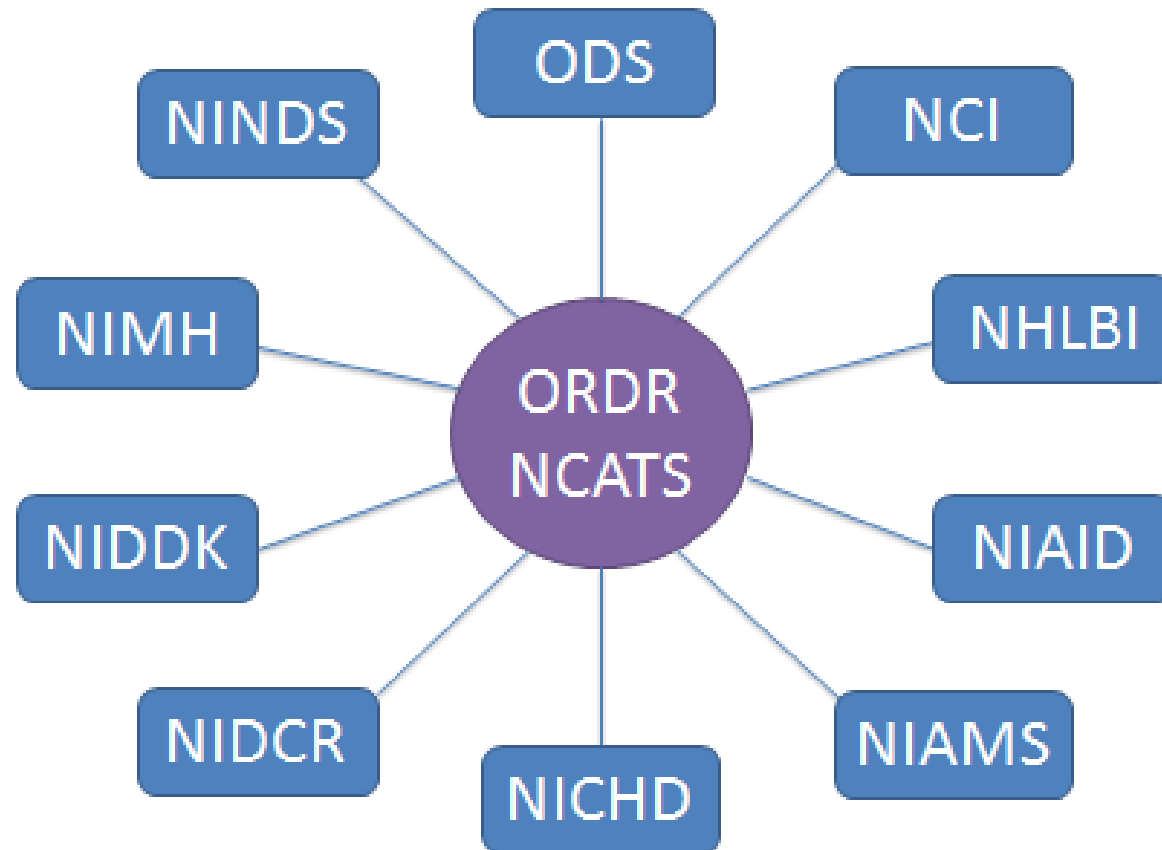
# RDCRN Program

The RDCRN is designed to advance medical research on rare diseases by providing support for clinical studies and facilitating collaboration, study enrollment and data sharing.

Through the RDCRN program consortia, physician scientists and their multidisciplinary teams work together with patient advocacy groups to study rare diseases at sites across USA and other countries.

# Led by NCATS (ORDR), Collaboration with 10 NIH Institutes

## RDCRN Program at NCATS



# RDCRN Program: Background Information

- Established (in 2003 by ORDR) in response to a Request for Application (RFA). Ten consortia a central Data Management and Coordinating Center (DMCC)
- Expanded in 2009 to 17 consortia and a DMCC (Reissuance of RFA)
- Each RDCRN Consortium : multiple diseases/ investigators / sites, collaborative clinical research Involving Patient Advocacy Groups (PAGs) as research partners

# RDCRN Program: Background Information

- *These are cooperative agreement (U54) awards for 5 years.* Scientific collaborators (project scientists) from ORDR, NCATS and NIH Institutes/Centers (ICs)
- Each awardee (Consortium) receives no more than \$1.25 M Total Cost/year for multi site studies
- RDCRN 3rd cycle (Renewed - 2014), an ORDR, NCATS Initiative

22 distinct multi-site Consortia and a DMCC

A Network of Network!

# Goals of the RDCRN Program

- Facilitate clinical research by:
  - Creating multi-site Consortia focused on a group of at least 3 related diseases
  - Making meaningful large-scale clinical studies possible
    - Longitudinal studies, Clinical Trials, Natural History Studies are required
    - Establishing uniform protocols for data collection
    - Cost sharing infrastructure
    - Centralized data repository and data sharing for rare diseases
- Collaborate with patients advocacy groups (as research partners)
- Train new investigators
- Support Pilot Projects Program
- Provide Website resource for education and research in rare diseases

## *Requirements*

# Special Features of RDCRN Program

- *The RDCRN is unique in its approach to addressing rare diseases as a group. Each consortium studies a group of minimum three related rare diseases.*
- *The direct involvement of PAGs as research partners is a major feature and requirement of this network.*
- NCATS (ORDR program)—Collaboration with 10 NIH ICs
  - Cooperative Agreement Awards managed by collaborating NIH IC (*culture change*)



# About RDCRN Program

- Collectively, the RDCRN is studying 200 rare diseases in natural history and clinical trials at 267 clinical sites located in the US and in 17 countries.
- There are more than 90 active protocols.
- 41,519 patients have enrolled in clinical studies.
- There have been 264 trainees.
- There are 3,261 collaborative consortium members.
- There are 144 PAGs as research partners, collectively formed a Coalition (RDCRN-CPAG).

<http://rarediseasesnetwork.epi.usf.edu/>

## ORDR/NCATS

(NCI, NHLBI, NIAID, NIAMS,  
NICHD, NIDCR, NIDDK, NIMH,  
NINDS, ODS)

Dystonia  
Coalition

Coalition of Patient  
Advocacy Groups  
(CPAG)

Porphyria Rare Disease Clinical  
Research Consortium

PAG

North America Mitochondrial  
Diseases Consortium

Primary Immune Deficiency  
Treatment Consortium

Brittle Bone Disorders  
Consortium

Chronic Graft Versus  
Host Disease

The Data Management and  
Coordinating Center

Urea Cycle Disorders  
Consortium

Brain Vascular  
Malformation Consortium

Genetic Disorders of  
Mucociliary Clearance

Consortium of Eosinophilic  
Gastrointestinal Disease Researchers

Rett, MECP2 Duplications  
and Rett-Related  
Disorders Consortium

Sterol and Isoprenoid  
Diseases Consortium

Autonomic Disorders  
Consortium

Clinical Research in ALS & Related  
Disorders for Therapeutic Development

Vasculitis Clinical  
Research Consortium

Rare Kidney  
Stone Consortium

Lysosomal  
Disease Network

Rare Lung Diseases  
Consortium

Nephrotic Syndrome  
Study Network

Inherited Neuropathies  
Consortium

The Frontotemporal Lobar  
Degeneration Clinical  
Research Consortium

Developmental Synaptopathies  
Associated with TSC, PTEN  
And SHANK3 Mutations

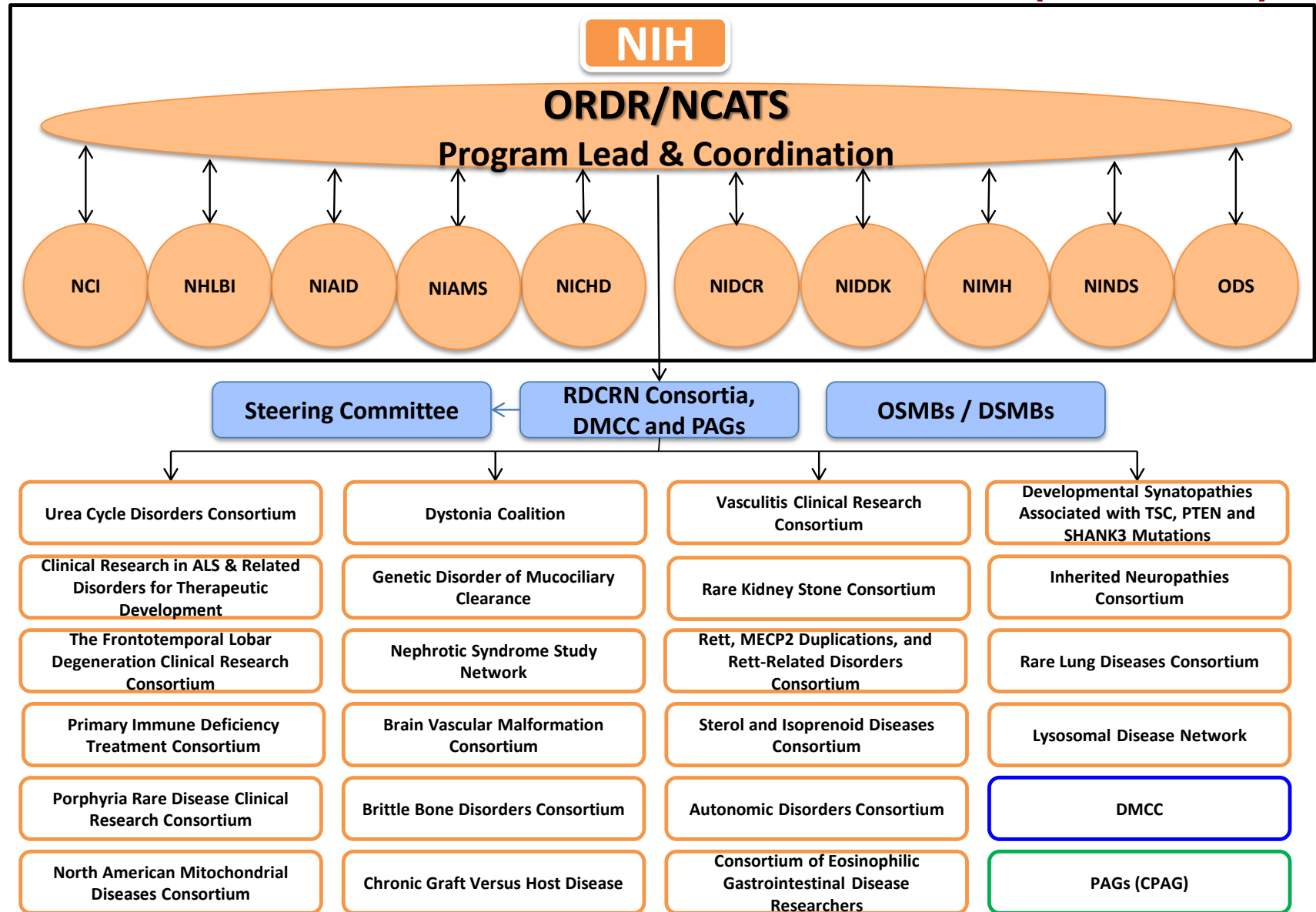


- Collaborative Clinical Research
- Centralized Data Coordination and Technology Development
- Public Resources and Education
- Training

# RDCRN Protocols

Type of Study	Number of Protocols
Pilot	17
Longitudinal	50
Phase I	1
Phase II	6
Phase III	4
IND	5
Industry Sponsored	12
Case Control	1
Chart Review	2

# Rare Disease Clinical Research Network 3 (RDCRN 3)



# Value of PAGs as Research Partners

*Since 2004 PAGs within RDCRN are involved in more than one of the following roles as research partners-*

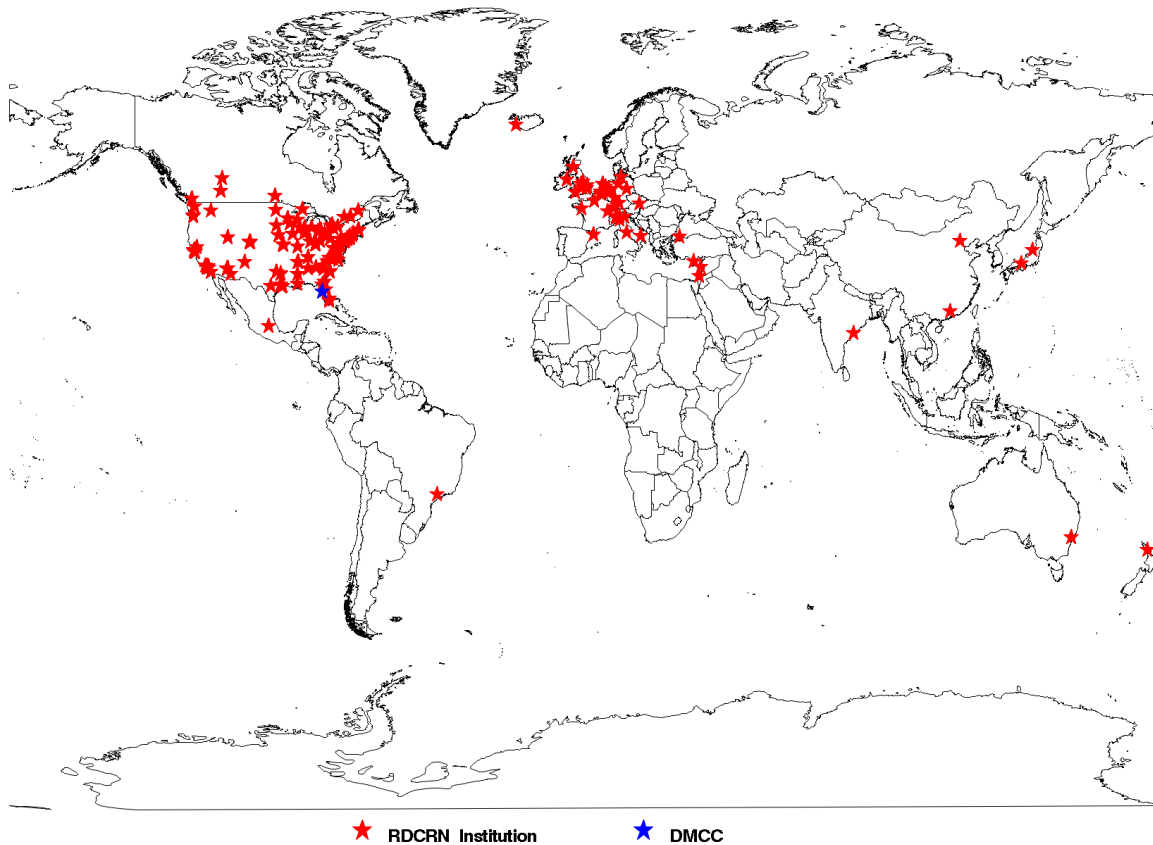
- Recruit patients for clinical studies, encourage participation in NHS
- Identify cohorts of patients with range of phenotypic expression
- Educate patients, public, media and health care providers
- Identify research efforts and translate research results to communities

# Value of PAGs as Research Partners

- Organize and fund research based Scientific conferences and meetings for patients/families/caregivers
- Provide financial support for research and training programs of RDCRN (consortia) and patient registries
- Provide financial support for *travel clinics* to facilitate patient access to investigators and studies
- Establish global partnership

# RDCRN International Sites

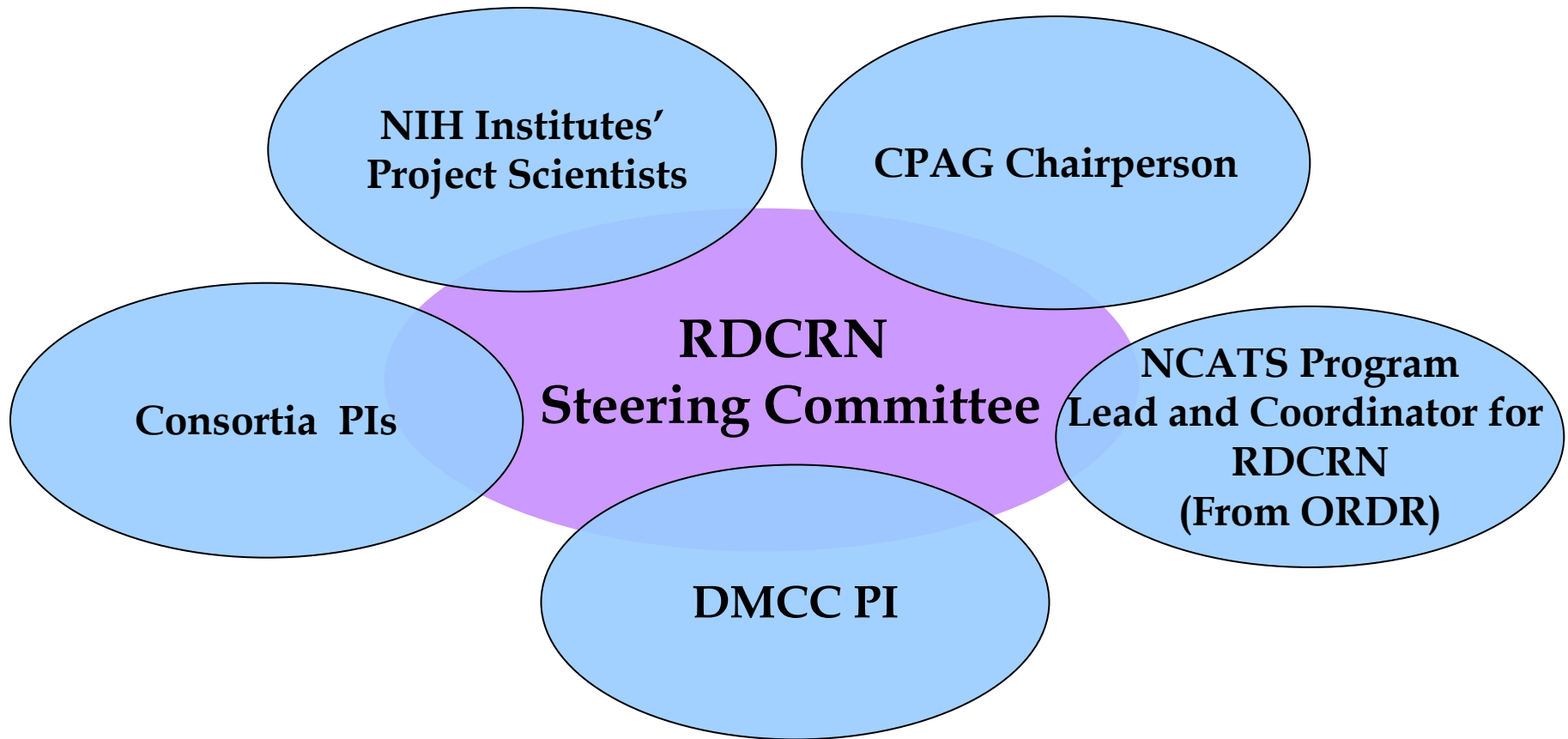
Data as of February 21, 2016



- Australia
- Belgium
- Canada
- England
- France
- Germany
- Iceland
- India
- Italy
- Netherlands
- Scotland
- Spain
- Switzerland
- China
- Japan

# RDCRN Steering Committee Organization

*(Review, facilitate and establish all Network procedures and functions)*





# Constant Communication for Collaboration!

- Monthly RDCRN Steering Committee calls, two in person meetings in Washington DC area (*CPAG chair*)
- Monthly meeting with NIH Institutes~50 medical officer and program officers
- Biweekly meetings with RDCRN-DMCC
- Quarterly calls with *RDCRN-CPAG*, in person
- Individual RDCRN-Consortium calls with *PAG's participation*

# RDCRN-Data Management and Coordinating Center (DMCC)

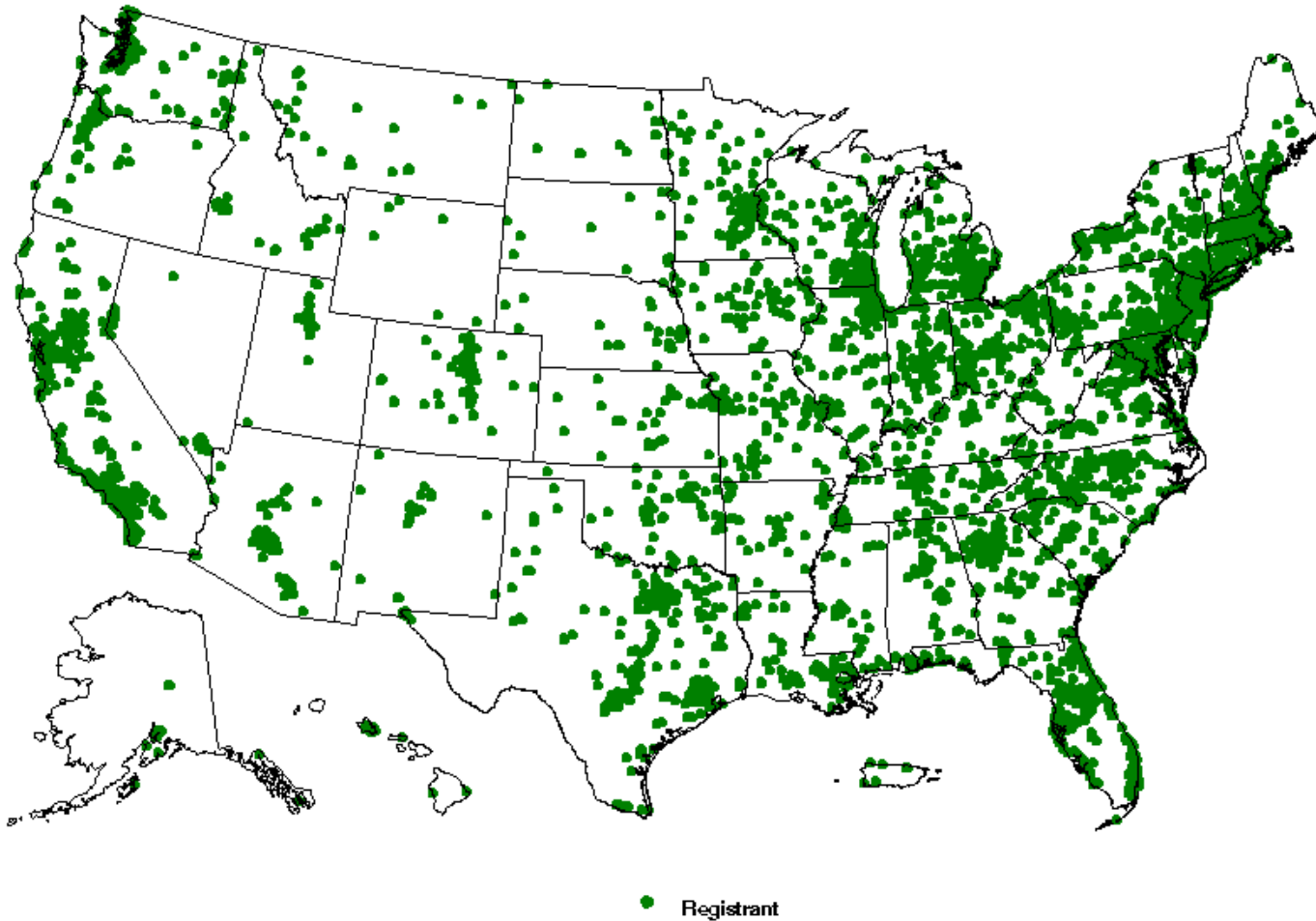
- Supports RDCRN by providing technologies, tools to collect clinical research data and support for study design and data analysis
- On-line protocol management system
  - Web-based patient enrollment (recruitment and referral)
  - Data entry and collection with data standards
  - Adverse event reporting
- Provides protocol training for research staff
- Works with the individual NIH Institutes' Data and Safety Monitoring Boards to establish protocols for Adverse Events notification and reporting
- Monitor Network protocol adherence, data collection and data submission

## Responsibilities of RDCRN DMCC (Cont.)

- Coordinates site visits for auditing individual consortia sites
- Provides a user-friendly web resource site for the public, research scientists, and clinicians; *involvement of PAGs* (>2 million hits/year)
- Maintain members' website, documentation and database
- *Oversees and maintains RDCRN Patient Contact Registry*

# RDCRN Contact Registry (2004)

## (U.S. Geographic Distribution of Contact Registrants)

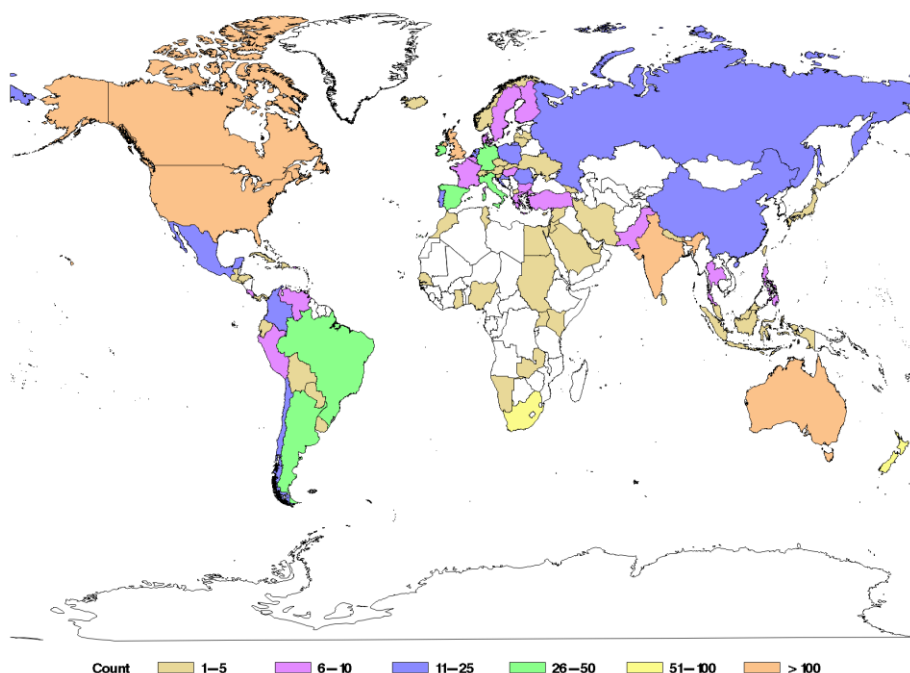


- Enrollment open to patients with diseases under study by Consortia

- Provides international on-line system for communication, recruitment, research

# RDCRN Contact Registry Overview

Data as of August 31, 2015



- 213 diseases represented
- 109 countries
- 16,512 total registrations
- 39% referred from PAGs
- 38% from internet
- 6% referred from med. prof.
- 260,000+ email communications

## Goals:

To inform registrants about RDCRN studies available;

To disseminate information about RDCRN activities

# **An Example of Collaboration/Scientific Advancements: The Urea Cycle Disorders Consortia at Children's National Medical Center**

- 19 Academic Research Centers in USA and 2 International Sites
- Collaborators With European Registry And Network For Intoxication Type Metabolic Disorders (EIMD)
- Industry Partnerships - 3 Products Approved
  - Ucyclyd Pharma: Ammonul
  - Recordati: Carbaglu
  - Hyperion: Ravicti
- Patient Advocacy Group - The National Urea Cycle Disorders Foundation
- Foundations - O'Malley Family Foundation, Kettering Fund, Rotenberg Family Foundation, and Dietmar-Hopp Foundation
- ORDR/NCATS and NICHD (from NIH), providing support and scientific collaboration

# Another Example: RDCRN-Rare Lung Diseases Consortium (RLDC)

- In early 2015 FDA accepted for priority review a supplemental New Drug Application for (sNDA) RAPAMUNE® for the treatment of lymphangioleiomyomatosis (LAM)
- LAM is a rare, progressive lung disease that primarily affects women of childbearing age that is often fatal. (March/2015 FDA approval)
- *This is the first drug approved for the treatment of LAM!*
- This is an accomplishment of the Multicenter International LAM Efficacy and Safety of Sirolimus (MILES) Trial (conducted by Dr. Francis McCormack of RDCRN RLDC in collaboration with LAM Foundation). The sNDA was based on results from the MILES Trial. (Wyeth)
  - *Collaborative effort!*

# Genetic Disorders of Mucociliary Clearance Consortium & Primary Ciliary Diskinesia (PCD) Foundation

- Diagnosis, monitoring, and treatment of primary ciliary dyskinesia: PCD foundation consensus recommendations based on state of the art review.
- Pediatric Pulmonology. September 29, 2015
- Shapiro AJ, Zariwala MA, Ferkol T, Davis SD, Sagel SD, Dell SD, Rosenfeld M, Olivier KN, Milla C, Daniel SJ, Kimple AJ, Manion M, Knowles MR, Leigh MW



# Through the RDCRN program.....

- New diagnostic methods have been generated
- New gene identification has been facilitated and
- New therapies have been identified.

by creating *collaborative multidisciplinary, multi-site research consortia* consisting of PAGs, academic researchers from domestic and international sites and project scientists from NIH as collaborators, the program has demonstrated that collaborative effort can accelerate clinical research.

# The RDCRN program.....

Has proven to be an effective model to

- Maximize investigator participation
- Initiate clinical trials
- Facilitate patient recruitment
- Accelerate young investigator training and
- Engage patient support

*enabling pharmaceutical industry and government sponsored research clinical studies to proceed with a supportive infrastructure to complete the clinical studies in a timely fashion.*

# Team Work!

- Clinical Sites
- Principal and co-investigators and the DMCC (multidisciplinary group)
- Trainees
- Study Coordinators
- Patient Advocacy Groups (PAGs)
- Pharmaceutical industry
- ORDR/NCATS and NIH Institutes staff (program officers and project scientists)
- *Patients*

**RDCRN: Working model for collaborative, multi-site clinical studies with PAGs partnership in an inexpensive way!**

**RDCRN consists of 267 sites, more than 144 PAGs and conducts research on more than 200 rare diseases**

# T. E. A. M.



# ***RDCRN: An Effective and Working Model for Collaborative Multi-Site Rare Diseases Research Efforts***



# Thanks for your attention!

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*(Program Director, RDCRN)*  
Office of Rare Diseases Research (ORDR), NCATS



# NCATS



# RDCRN Homepage

For Patients  
and  
Families



## Find Patient Advocacy Groups

The Coalition of Patient Advocacy Groups (CPAG) represents the perspective and interests of all patient advocacy organizations associated with the diseases we study.

 **Stay Connected -  
Join the Contact  
Registry**

For  
Healthcare  
Professionals



## Training Opportunities

## Other Rare Disease Initiatives

About Us



## What is the RDCRN?

Aims of the Rare Diseases Clinical  
Research Network

**Contact Us**