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NIH National Institute of Neurological Disorders and Stroke

RARE DISEASES CLINICAL RESEARCH NETWORK

Tiina K. Urv, Ph.D.

NIH – NCATS

Office of Rare Diseases Research

NIH National Center for Advancing Translational Sciences

RARE DISEASES
CLINICAL RESEARCH NETWORK

Established by Rare Diseases Act of 2002
(Public Law 107-280)

*"planning, establishing, or strengthening, and providing basic operating support for **regional centers of excellence** for clinical research into, training in, and demonstration of diagnostic, prevention, control, and treatment methods for rare diseases"*

Established 2003
Recompeted every 5 years

Division of Rare Diseases Research Innovation

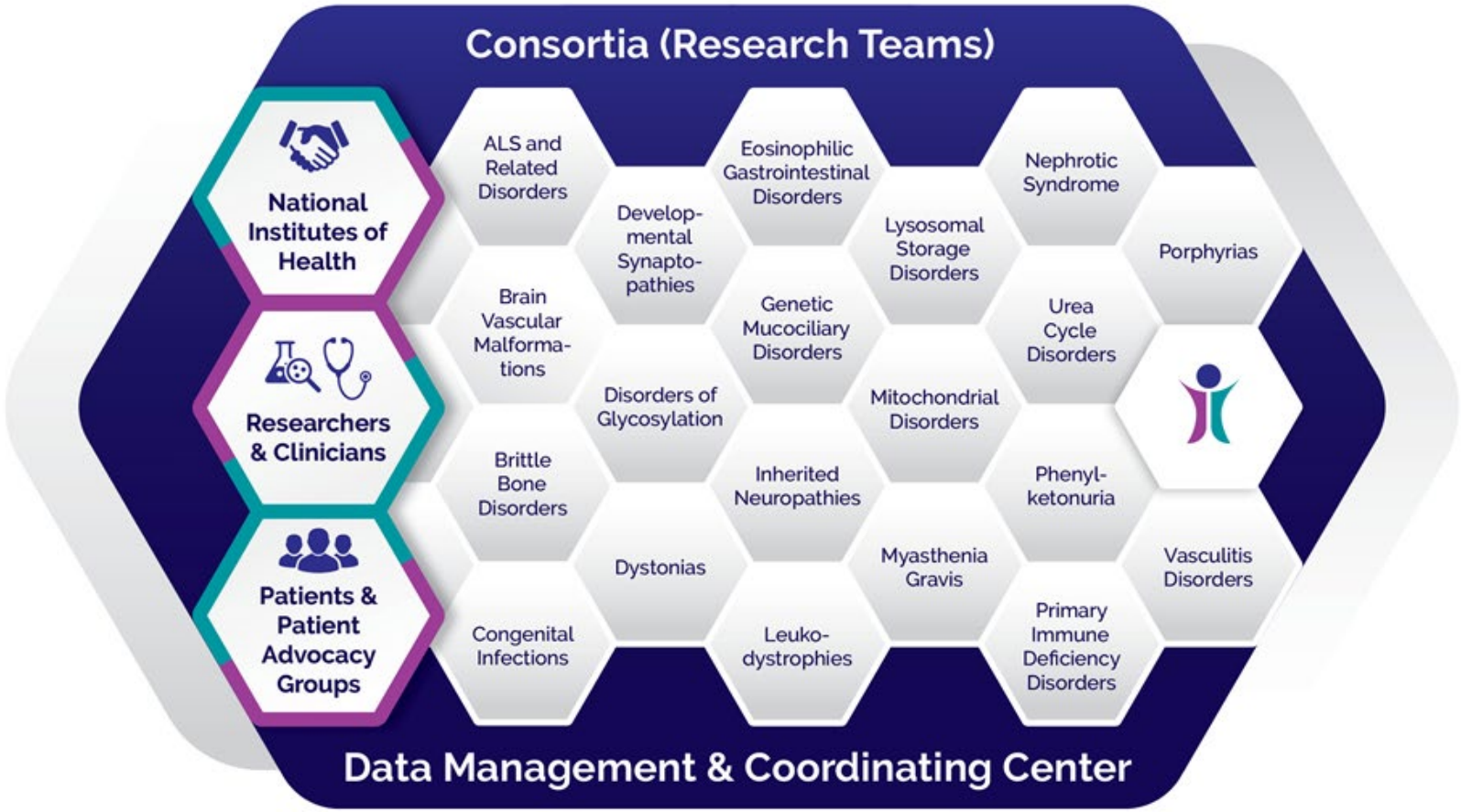
Tiina Urv, Ph.D
Program Director

Joanne Lumsden, Ph.D.
Scientific Program Manager

Consortium Acronym	Consortium Name	RDCRN1 2003-2008	RDCRN2 2009-2013	RDCRN3 2014-2018	RDCRN4 2019-2023
GDMCC	Genetic Disorders of Mucociliary Clearance Consortium	X	X	X	X
UCDC	Urea Cycle Disorders Consortium	X	X	X	X
VCRC	Vasculitis Clinical Research Consortium	X	X	X	X
PC	Porphyrias Consortium		X	X	X
NAMDC	North American Mitochondrial Disease Consortium		X	X	X
DC	Dystonia Coalition		X	X	X
BVMC	Brain Vascular Malformation Consortium		X	X	X
NEPTUNE	Nephrotic Syndrome Study Network		X	X	X
PIDTC	Primary Immune Deficiency Treatment Consortium		X	X	X
INC	Inherited Neuropathy Consortium		X	X	X
LDN	Lysosomal Disease Network		X	X	X
CReATe	Clinical Research in ALS and Related Disorders for Therapeutic Development			X	X
BBDC	Brittle Bone Disorders Consortium			X	X
CEGIR	Consortium of Eosinophilic Gastrointestinal Disease Researchers			X	X
DSC	Developmental Synaptopathies Consortium			X	X
PHEFREE	Phenylalanine Families and Researchers Exploring Evidence				X
MGNet	Myasthenia Gravis Rare Disease Network				X
CPIC	Congenital and Perinatal Infections Consortium				X
FCDGC	Frontiers in Congenital Disorders of Glycosylation				X
GLIA-CTN	Global Leukodystrophy Initiative Clinical Trials Network				X
RTT	Rett Syndrome, MECP2 Duplications, and Rett-related Disorders Consortium	X	X	X	
RKSC	Rare Kidney Stone Consortium		X	X	
STAIR	Sterol and Isoprenoid Diseases Consortium		X	X	
ADC	Autonomic Disorders Consortium		X	X	
RLDC	Rare Lung Diseases Consortium	X		X	
ARTFL	Advancing Research and Treatment for Frontotemporal Lobar Degeneration Consortium			X	
CINCH	Clinical Investigation of Neurologic Channelopathies	X	X		
SGCC	Salivary Gland Carcinomas Consortium		X		
cGVHD	Chronic Graft Versus Host Disease Consortium (cGVHD)		X		
BMFC	Bone Marrow Failure Consortium	X			
RGSDC	Rare Genetic Steroid Disorders Consortium	X			
RTDC	Rare Thrombotic Diseases Consortium	X			
CLiC	Cholestatic Liver Disease Consortium	X			

RARE DISEASES
CLINICAL RESEARCH NETWORK

A network of 20 research teams collaborating to achieve faster diagnosis and better treatments for patients with rare diseases



National Center for Advancing Translational Sciences | National Institute of Neurological Disorders and Stroke | National Institute of Allergy and Infectious Diseases | National Institute of Diabetes and Digestive and Kidney Diseases | *Eunice Kennedy Shriver* National Institute of Child Health and Human Development | National Institute of Arthritis and Musculoskeletal and Skin Diseases | National Heart, Lung, and Blood Institute | National Institute of Dental and Craniofacial Research | National Institute of Mental Health | Office of Dietary Supplements

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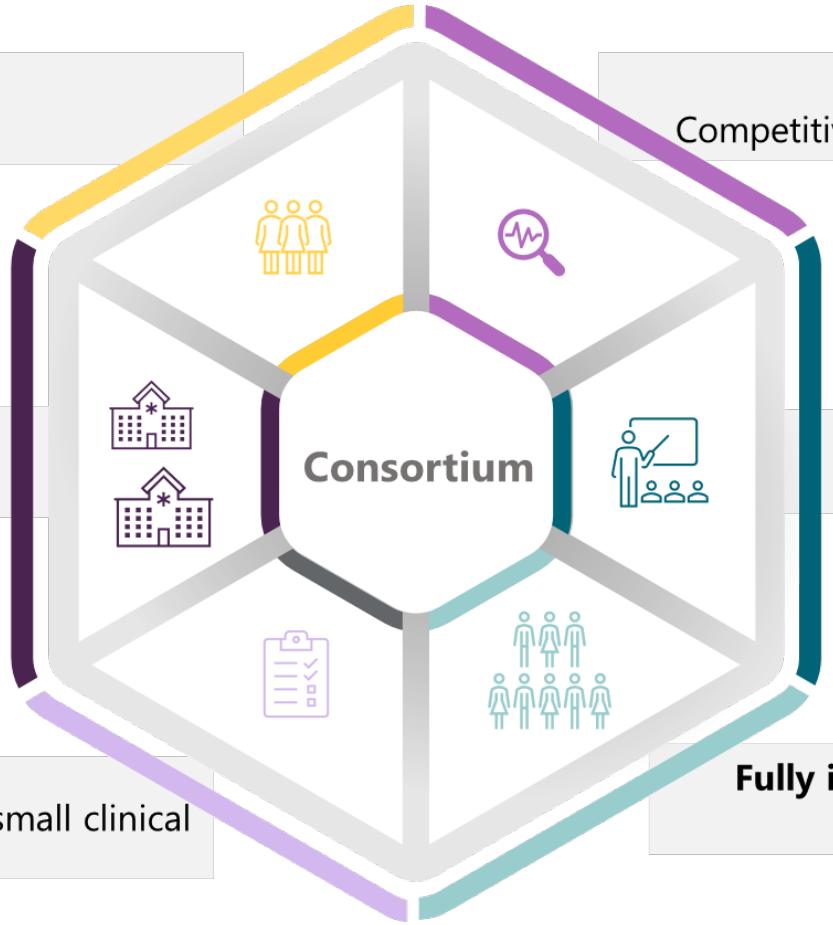
Rare Diseases Clinical Research Consortium

Three or more disorders
Mean = 9 disorders

Pilot Studies
Competitive within the consortium's discretion



Multiple sites
Mean =19 sites Range – 5 - 42

Career enhancement core.
e.g., Competitive scholar awards

Three – Five clinical studies
e.g., Natural History, biomarkers, small clinical trials, outcome measures

Fully integrated patient advocacy group
Mean = 9 Range 1-60

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RARE DISEASES CLINICAL RESEARCH NETWORK

RDCRN Clinical Sites

Active Sites	Unique Locations
358	197

Site	# of consortia
Children's Hospital of Philadelphia	9
Baylor College of Medicine	8
Mayo Clinic	8
University of Minnesota	8
University of Utah	8
Children's Hospital Colorado	7
Seattle Children's Hospital	7
Stanford University	7
Boston Children's Hospital	6
Children's National Medical Center	6
Duke University	6
Massachusetts General Hospital	6
Washington University in St. Louis	6
Cleveland Clinic	5
Johns Hopkins University	5
University of Alabama at Birmingham	5
University of California, Los Angeles	5
University of California, San Francisco	5
University of Miami	5
University of Pennsylvania	5

Country	# of sites
Australia	2
Belgium	1
Canada	18
England	13
Germany	3
India	1
Ireland	1
Italy	2
Netherlands	1
South Africa	1
Switzerland	1

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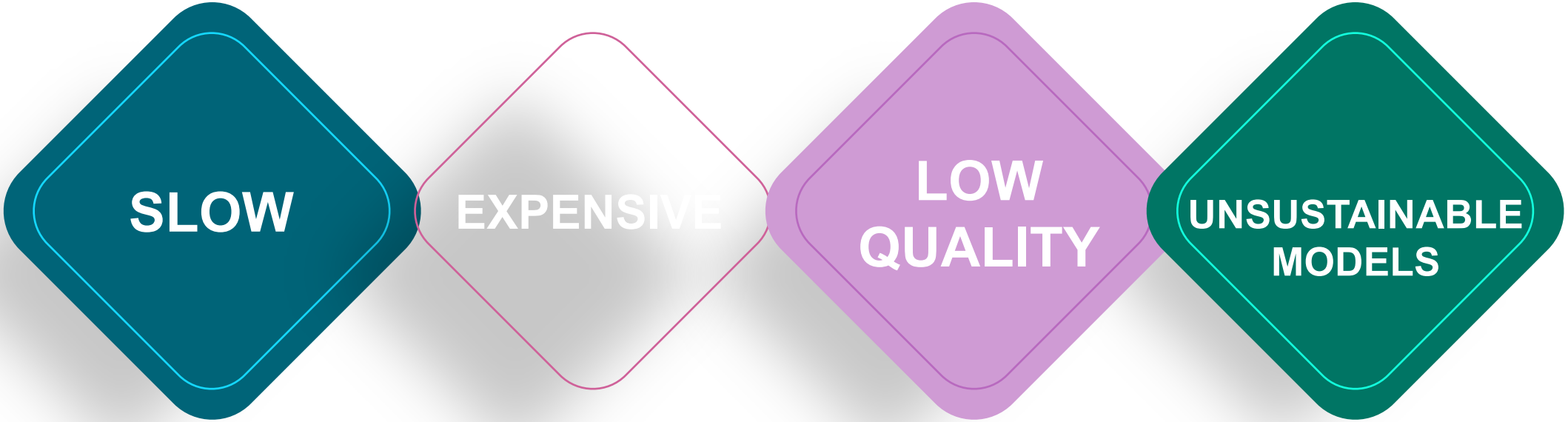
Challenges of Developing Treatments for Rare Diseases

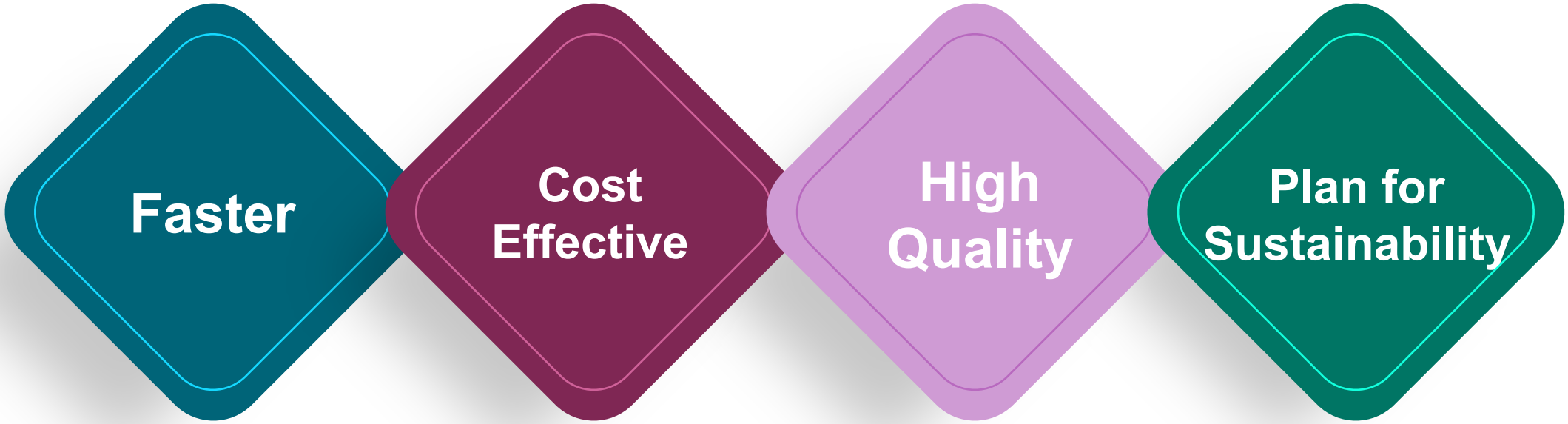


A novel drug can take 10 – 15 years to develop

Clinical development cost in the range of 2 Billion dollars

95% of human studies fail

Cost+ Expense+ Quality = Unsustainable


Faster
Cost Effective
High Quality
Plan for Sustainability

Faster

Strategies

Networks Established
- Clinical Research
- Patient Advocacy

Natural History Studies

Tools Established
- Outcome Measures
- Biomarkers
- Common Data Elements

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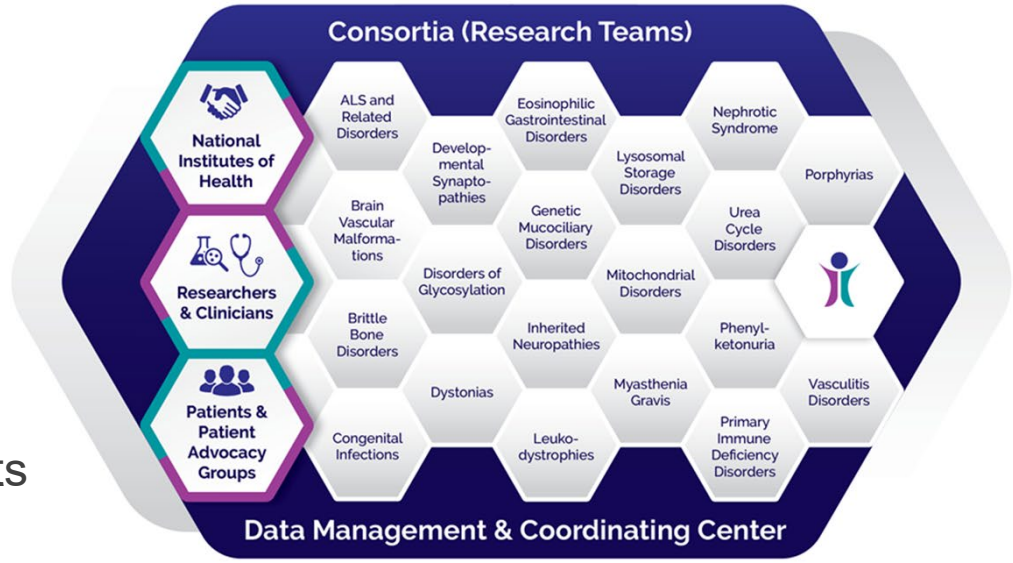

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RISK

Clinical Trial Readiness

WHY

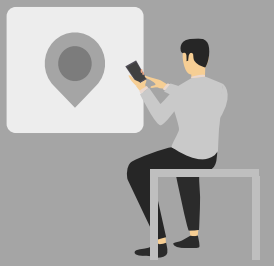
Why is this the best way to go forward? Show me the data!

WHAT

What is the best potential treatment?

What is the desired outcome

WHERE



Where are the experts?
Where are the patients?

WHEN

When is the best time to treat a condition?

Do we have everything in place?

WHO

Who do you treat?

Who will conduct the trial?

HOW

How should the trial be conducted?

Cost Effective

Strategies

Economies of Scale

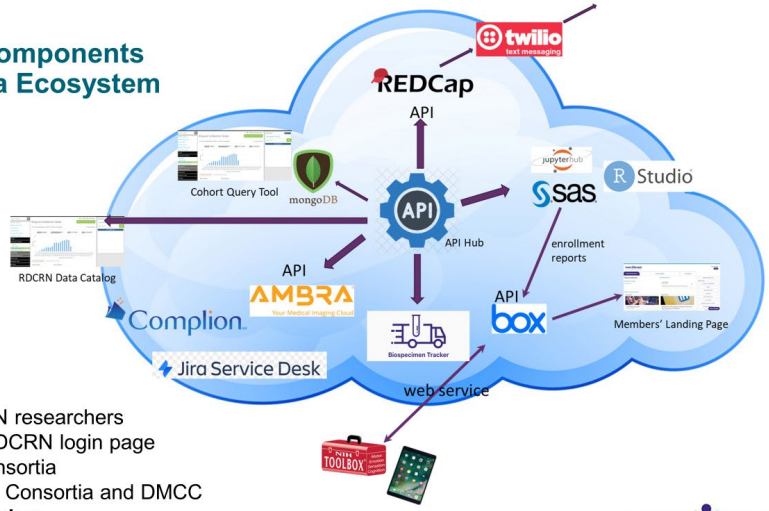
- Shared work environment
- Shared tools

Innovative Models for Trials

- Basket trials
- Umbrella trials

Operational Environment

Turning Components into a Data Ecosystem



OPEN FOR BUSINESS

Audience: RDCRN researchers
Authentication: RDCRN login page
Authorization: Consortia
Data governance: Consortia and DMCC
***Internal* data sharing**

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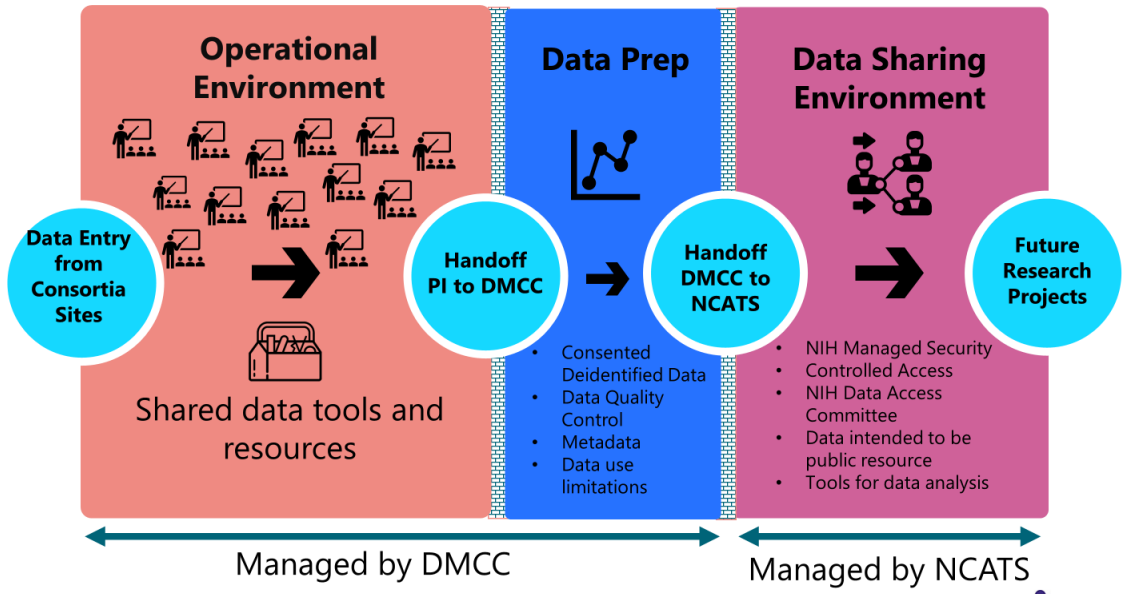
High Quality

Strategies

Data Standards
- FAIR Principles
- Good data practices

Research
- Scientific Rigor
- Reproducibility
- Transparency



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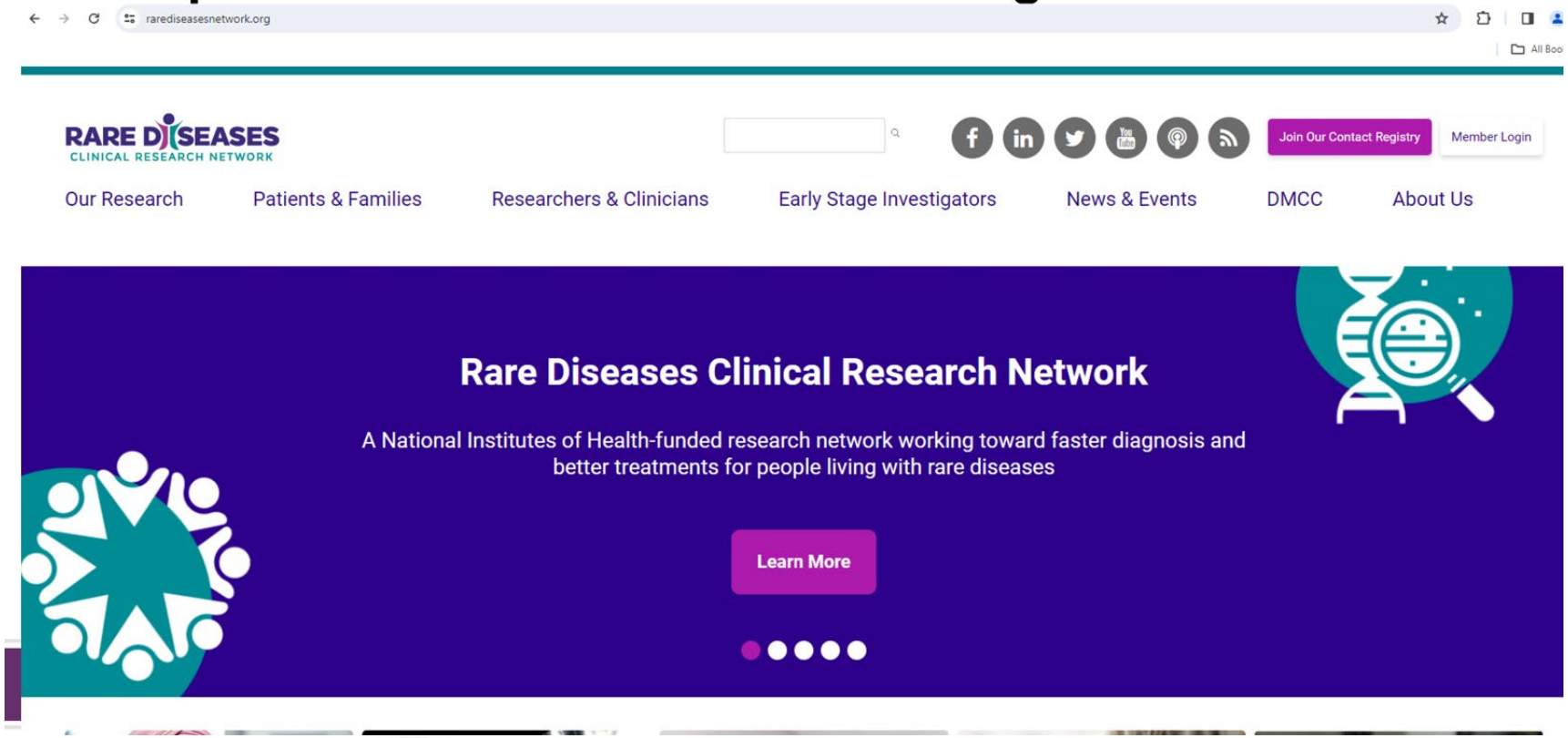
Plan for Sustainability

https://www.rarediseasesnetwork.org/



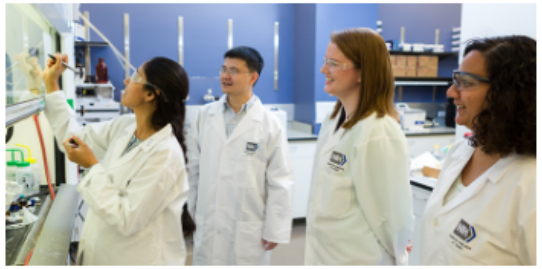
Rare Diseases Research Activities

We are addressing the public health challenges posed by rare diseases through a variety of collaborative research efforts.

Bespoke Gene Therapy Consortium

The Bespoke Gene Therapy Consortium (BGTC) focuses on developing platforms and standards to speed the development and delivery of gene therapies for rare diseases.

Learn More



Therapeutics for Rare and Neglected Diseases (TRND)

The TRND program moves basic research discoveries in the lab closer to becoming new drugs.

Learn More

Rare Diseases Clinical Research Network (RDCRN)

The RDCRN brings scientists together with rare disease organizations to study more than 200 rare diseases at sites across the country.

Learn More

See All Rare Diseases Activities

Accelerating Rare disease Cures (ARC) Program

CDER's ARC Program | Center for Drug Evaluation and Research

Accelerating Rare disease Cures (ARC) Program

CDER's Accelerating Rare disease Cures (ARC) Program brings together CDER's collective expertise and activities to provide strategic overview and coordination of CDER's rare disease activities. The ARC Program is governed by leadership from across CDER's Office of the Center Director, Office of New Drugs, and the Office of Translational Sciences. The program is managed by CDER's Rare Diseases Team.

Vision: Speeding and increasing the development of effective and safe treatment options addressing the unmet needs of patients with rare diseases.

Mission: To drive scientific and regulatory innovation and engagement to accelerate the availability of treatments for patients with rare diseases.

Connect with us!

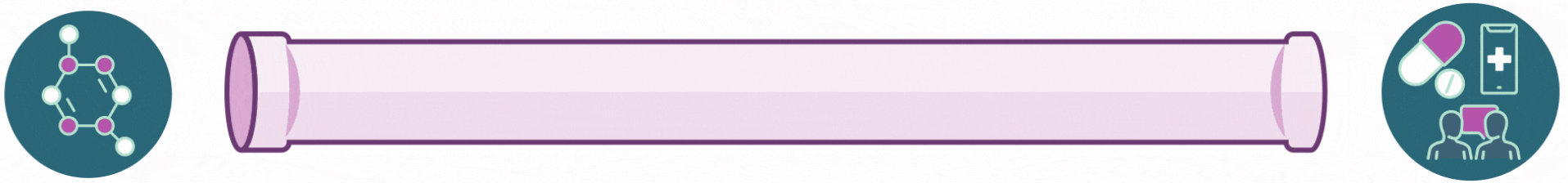
CDER_ARC_Program@fda.hhs.gov

CDER Rare Disease News

Content current as of:
12/21/2023

The Translational Pipeline

RDCRN addresses longstanding bottlenecks in the road to developing treatments, to accelerate progress to health solutions -- so that new treatments reach people faster



Operational **Financial/Administrative** **Scientific**

Bottlenecks:	RDCRN Solutions:
▪ Slow	▪ Consortia, Patient Advocacy Involvement, Natural History Studies, Outcome measures, Biomarkers
▪ Expensive	▪ Economies of Scale, Shared Tools, Shared Work Environment
▪ Poor quality Data	▪ Good data practices, FAIR Principles, Scientific Rigor, Reproducibility and Transparency

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RARE DISEASES CLINICAL RESEARCH NETWORK

RDCRN Cycle 4: 2019-2024

RARE DISEASES CLINICAL RESEARCH NETWORK

20
Research groups

170
Patient advocacy partners

10
NIH Institutes and Centers

295
Clinical sites in
37
U.S. States

10
Countries outside the U.S.

>200
Diseases studied

80
Clinical studies

13
Clinical trials

1101
Publications

16958
Academic citations

84
Policy document citations

* **2010-2024**

12
FDA-approved products for
11
rare diseases*

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RDCRN Translational Impact

RARE DISEASES CLINICAL RESEARCH NETWORK

Clinical Trials directly funded by U54 grant

- Predominantly small **Phase 1/Phase 2**
- Currently 18 trials funded in RDCRN4
- Primarily repurposed drugs, diets, supplements, procedures, devices, some novel drugs

RDCRN-associated Clinical Trials

- Predominantly **Phase 2/Phase 3**
- Funded by industry, IC-specific grants, FDA, PAGs
- Leveraging disease phenotype, patient population, clinical sites, endpoints, biomarkers, early phase safety and efficacy data
- *No NCATS $$ involved*

12 FDA-approved treatments for rare diseases

Consortium	Drug	Other Name	Indication	Company	Approval Date
UCDC	CARBAGLU®	carglumic acid	N-acetylglutamate synthetase (**NAGS**) deficiency	Orphan Europe	March 2010
VCRC	RITUXAN®	rituximab in combination with corticosteroids	Wegener's granulomatosis (**WG**) and microscopic polyangiitis (**MPA**)	Genentech and Biogen	April 2011
UCDC	RAVICTI®	glycerol phenylbutyrate	urea cycle disorders (**UCD**)	Hyperion Therapeutics	February 2013
RLDC	RAPAMUNE®	sirolimus	lymphangioleiomyomatosis (**LAM**)	Pfizer	May 2015
PC	SCENESSE®	afamelanotide	erythropoietic protoporphyria (**EPP**)	Clinuvel	October 2019
PC	GIVLAARI®	givosiran	acute hepatic porphyria (**AHP**)	Alnylam Pharmaceuticals	November 2019
RKSC	OXLUMO®	lumasiran	primary hyperoxaluria type 1 (**PH1**)	Alnylam Pharmaceuticals	November 2020
CEGIR	DUPIXENT®	dupilumab	eosinophilic esophagitis (**EoE**)	Regeneron	May 2022 Jan 2024 (pediatric)
RTT	DAYBUE™	trofinetide	**Rett** syndrome	Acadia Pharmaceuticals	March 2023
MGNet	RYSTIGGO®	rozanolixizumab-noli	generalized myasthenia gravis (**gMG**)	UCB	June 2023
RKSC	RIVFLOZA™	nedosiran	primary hyperoxaluria type 1 (**PH1**)	Novo Nordisk	October 2023

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