



# Rare Disease Research Overview

Lucia Monaco, Chair, International Rare Diseases Research Consortium Assembly

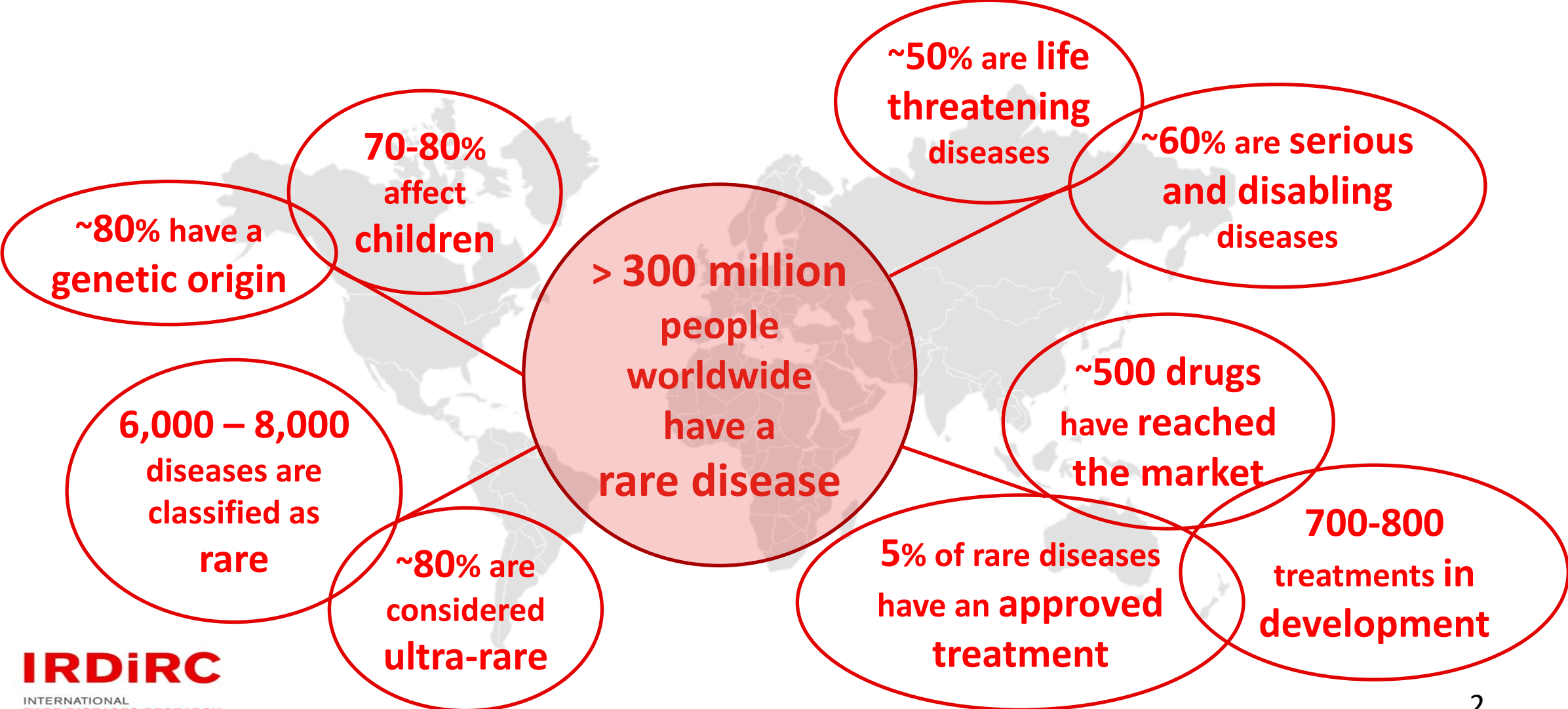
**NATIONAL PRESS FOUNDATION**

Online Workshop

**Covering Rare Diseases**

13 September 2021

# Rare disease scenario



# Rare disease disparities

## ▶ Diverse

- legal recognition / definition
- disease nomenclature

## ▶ Scattered

- scientific knowledge
- financial resources
- clinical competence

## ▶ Different

- geographic and socio-economic settings

## ▶ Uneven

- diagnostic tests available
- treatments available
- access to diagnosis and care

# Rare disease research challenges

## ▶ Access to patients

- ↪ Clinical data
- ↪ Biological material
- ↪ Patient consent

## ▶ Basic / preclinical research

- ↪ Data harmonization and sharing
- ↪ Funding
- ↪ Coordination / cooperation

## ▶ Translational research/ drug development

- ↪ Patient recruitment in clinical trials
- ↪ Clinical study design
- ↪ Regulatory requirements
- ↪ Profitability / sustainability

## ▶ Patient access to treatments

- ↪ Marketing authorization
- ↪ Pricing
- ↪ Health system approval

# Rare disease stakeholders – and stakes

## Players

- ▶ People living with a rare disease
- ▶ Researchers
- ▶ Companies
- ▶ Regulators
- ▶ Health Systems

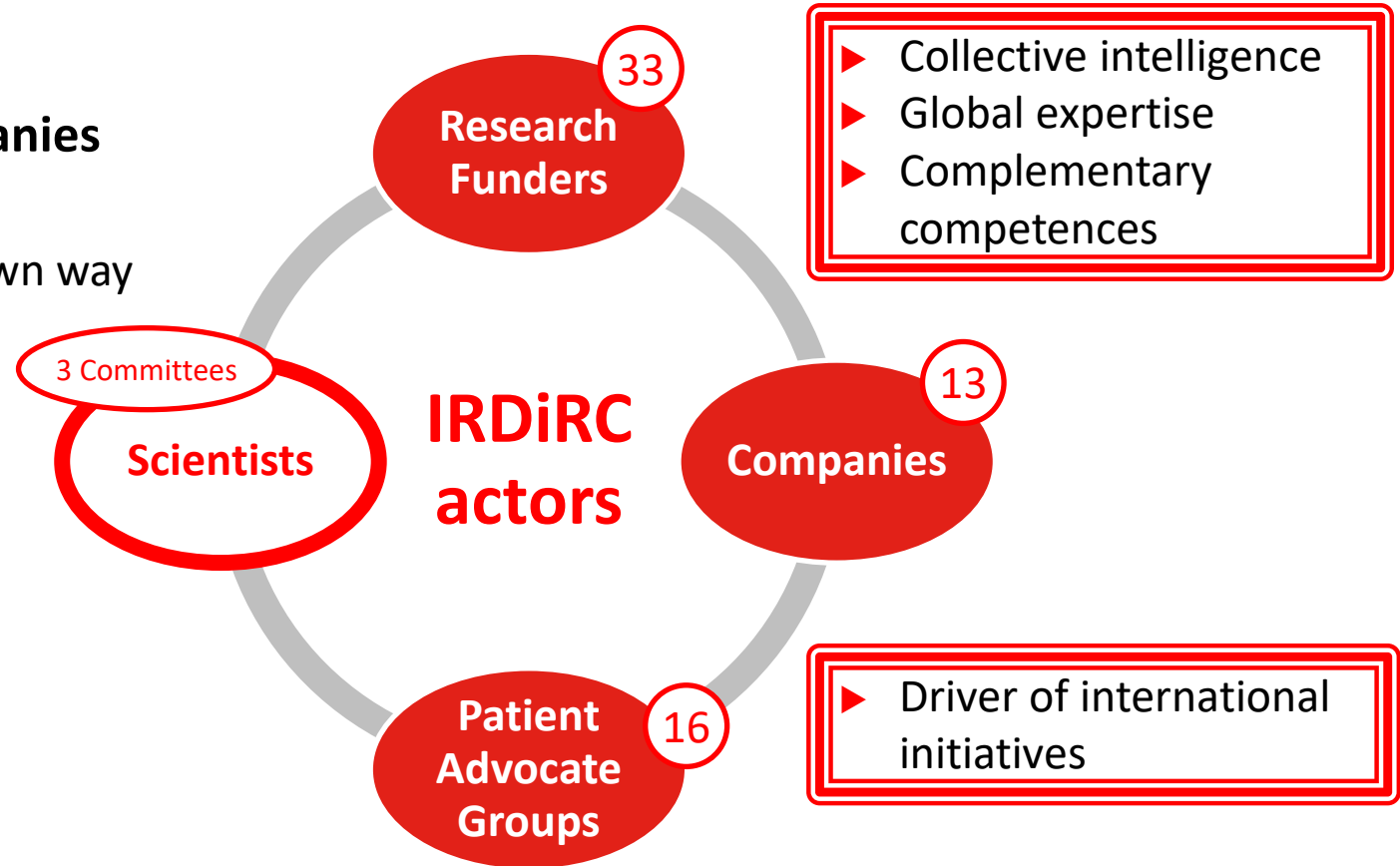
## Drivers

- ▶ Solutions (diagnosis & treatments)
- ▶ Discovery
- ▶ Profit
- ▶ Safety
- ▶ Sustainability

# International Rare Diseases Research Consortium (IRDiRC)

International level co-operation to stimulate, better coordinate & maximize output of rare disease research efforts around the world

- ▶ Launched in 2011
- ▶ Teams up **research funders** and **companies** investing in RD research
  - ↪ Each organization funds research its own way
  - ↪ Funded projects adhere to a common framework
- ▶ Umbrella **patient advocacy groups**
- ▶ **3 Scientific Committees**
  - ↪ Diagnostics
  - ↪ Therapies
  - ↪ Interdisciplinary



Countries hosting IRDiRC Member Organizations

Countries associated to IRDiRC Member Organizations

International

- Rare Diseases International (RDI)

# 62 IRDiRC Member Organizations from 22 Countries

- ▶ Europe 23
- ▶ North America 21
- ▶ Asia 11
- ▶ Africa 3
- ▶ Oceania 3
- ▶ South America 1

Europe

- Agence nationale de la recherche (ANR)
- Chiesi Farmaceutici
- European Commission (EC)
- RORDIS-Rare Diseases Europe
- Federal Ministry of Education and Research (BMBF)
- Fondazione Telethon (FTELE)
- French Foundation for Rare Diseases (FFRD)
- French Muscular Dystrophy Association (AFM-Téléthon)
- Georgian Foundation for Genetic and Rare Diseases
- Institute of Health Carlos III (ISCIII)
- Istituto Superiore di Sanità (ISS)
- LouLou Foundation
- Lysogene SA
- National Institute for Health Research (NIHR)
- National Institute of Health and Medical Research (INSERM)
- Roche Biotechnology
- The Netherlands Organisation for Health Research and Development (ZonMw)
- Ultragenyx Pharmaceutical Inc.
- **Innoskel**

North America

- Canadian Institutes for Health Research (CIHR)
- Canadian Organization for Rare Disorders (CORD)
- Cydan II, Inc.
- FDA Office of Orphan Products Development (FDA/OOPD)
- Genetic Alliance
- Genome Canada
- Global Genes
- National Cancer Institute (NCI)
- National Center for Advancing Translational Sciences (NCATS)
- National Eye Institute (NEI)
- National Human Genome Research Institute (NHGRI)
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
- National Institute of Child Health and Human Development (NICHD)
- National Institute of Dental and Craniofacial Research (NIDCR)
- National Institute of Neurological Disorders and Stroke (NINDS)
- National Organization for Rare Disorders (NORD)
- Pfizer Inc.
- Recursion Pharmaceuticals
- Sanford Research
- Takeda Pharmaceuticals
- Illumina, Inc.
- **Chan Zuckerberg Initiative**

Latin America

- Iberoamerican Alliance for Rare Diseases (ALIBER)

Africa

- Botswana Organization for Rare Diseases (BORDIS)
- Rare Disease Ghana Initiative (RDGI)
- Rare Diseases South Africa

Asia Pacific

- Asia Pacific Alliance for Rare Disease Organisations (APARDO)

Australia

- Rare Voices Australia (RVA)
- Western Australian Department of Health

Asia

- Advocacy Service for Rare and Intractable Diseases' multi-stakeholders in Japan (ASrid)
- BGI Genomics, China
- Chinese Organization for Rare Disorders (CORD)
- Indian Organization for Rare Diseases (I-ORD)
- Japan Agency for Medical Research and Development (AMED)
- Korea National Institute of Health (KNIH)
- National Rare Diseases Registry System of China (NRDRS)
- Organization for Rare Diseases India (ORD-I)
- Saudi Human Genome Project (SHGP)



Stay updated on <https://irdirc.org/>

# IRDiRC policies and guidelines

## Policies

main principles IRDiRC members agree to follow

## Guidelines

recommendations that offer advice as to “best practices”

## Key policies for research funders

- ▶ Promote **discovery of genes** underlying RDs
- ▶ Encourage **development of therapies**
- ▶ Encourage and facilitate rapid **data release**
- ▶ Promote **data** harmonization, interoperability and access to **registries and biobanks**
- ▶ Promote **coordination** between human and model systems research
- ▶ **Involve patients in all relevant aspects of RD research**

## Key policies for researchers

- ▶ Perform **collaborative research**, share data and results, avoid duplication
- ▶ Make **registries and biobanks interoperable** and harmonized, with a global scope
- ▶ **Share and distribute** RD biomaterial through **biobanks**
- ▶ **Exchange scientific and regulatory information** on clinical research
- ▶ **Balance IP issues with the need to share information** to the benefit of the research and patient community
- ▶ Adhere to and develop **research standards**
- ▶ **Publish results in a timely manner** on peer-reviewed and possibly open access journals



# IRDiRC Vision and Goals, by 2027

## Vision

Enable all people living with a rare disease to **receive** an accurate **diagnosis, care,** and available therapy **within one year** of coming to medical attention

## Goals

1. All patients coming to medical attention with a suspected rare disease will be **diagnosed within one year** if their disorder is known in the medical literature; all currently undiagnosable individuals will enter a globally coordinated **diagnostic and research pipeline**
2. **1000 new therapies** for rare diseases will be approved, the majority of which will focus on diseases without approved options
3. Methodologies will be developed to **assess the impact of diagnoses and therapies** on rare diseases patients

URGENCY  
ACCESS

DIAGNOSIS

THERAPIES

IMPACT

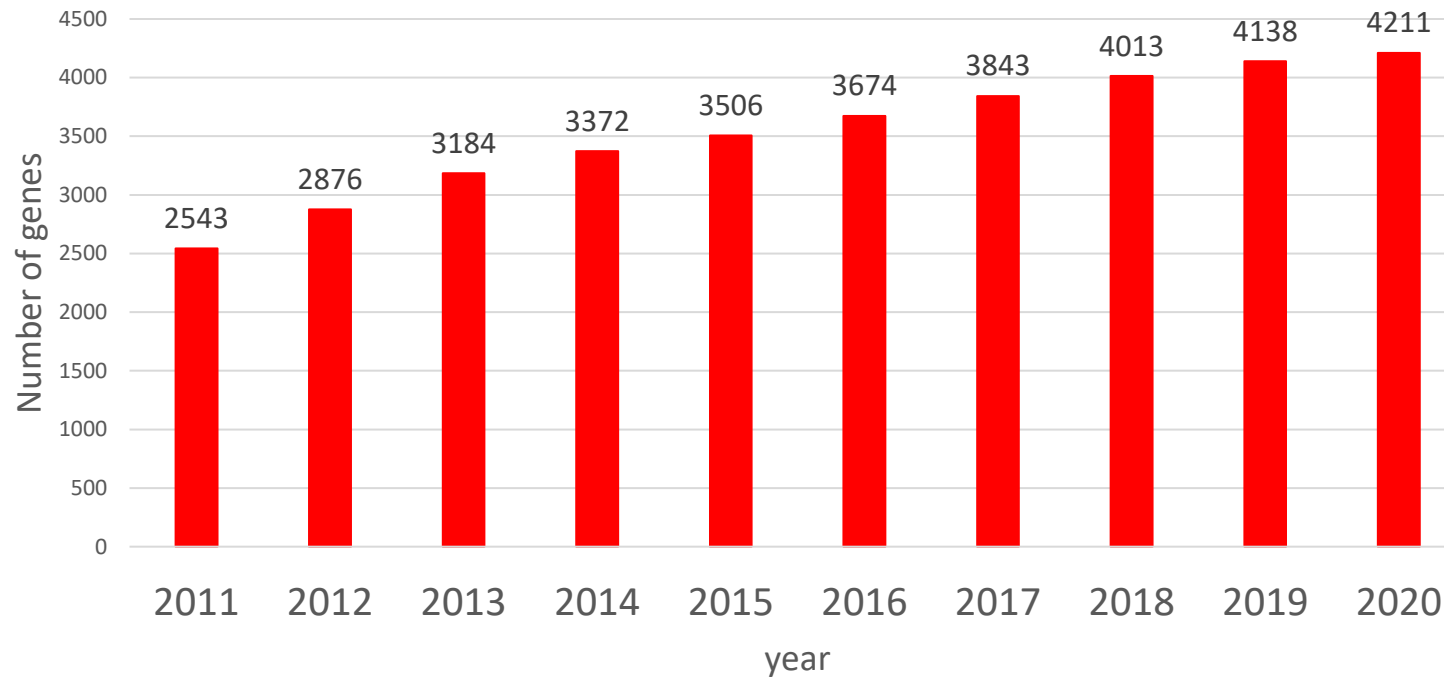


**IRDiRC**

INTERNATIONAL  
RARE DISEASES RESEARCH  
CONSORTIUM

# Progress towards IRDiRC Goal 1

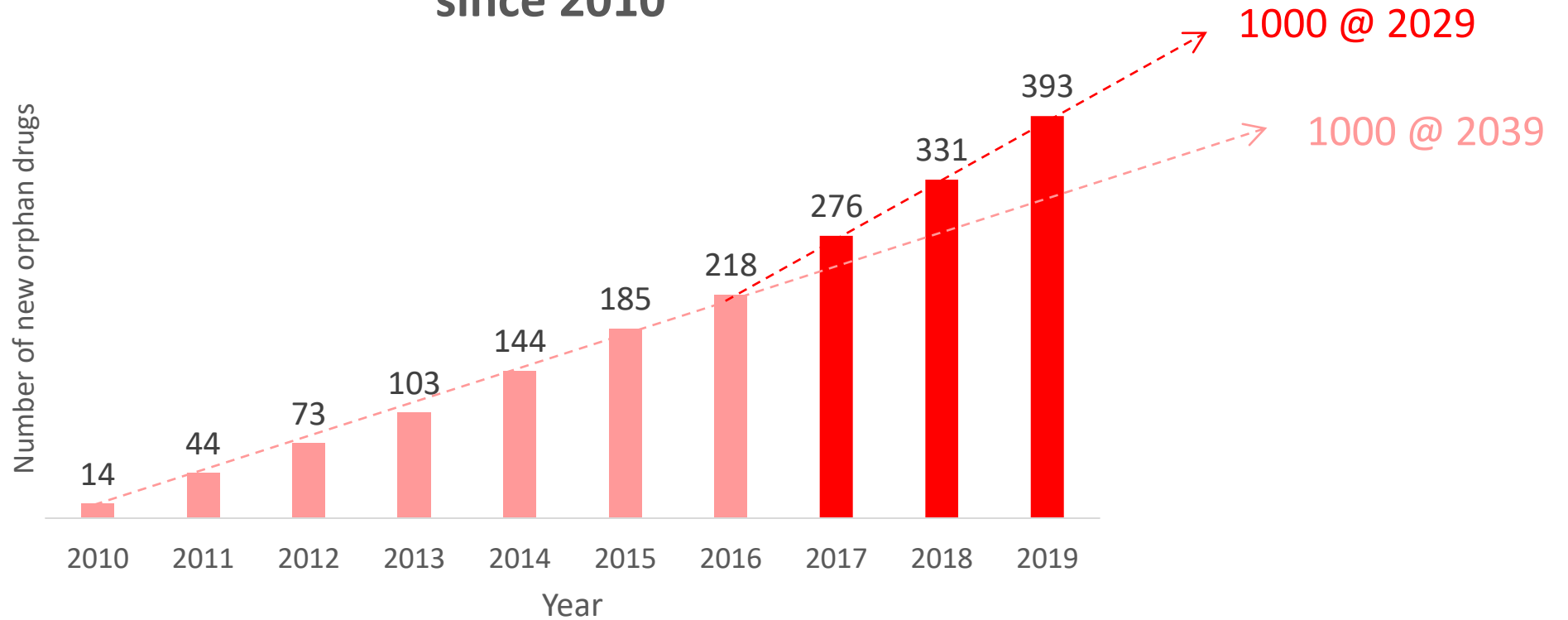
Cumulative number of genes linked to rare diseases since 2010



<https://irdirc.org/research/rd-metrics/>

# Progress towards IRDiRC Goal 2

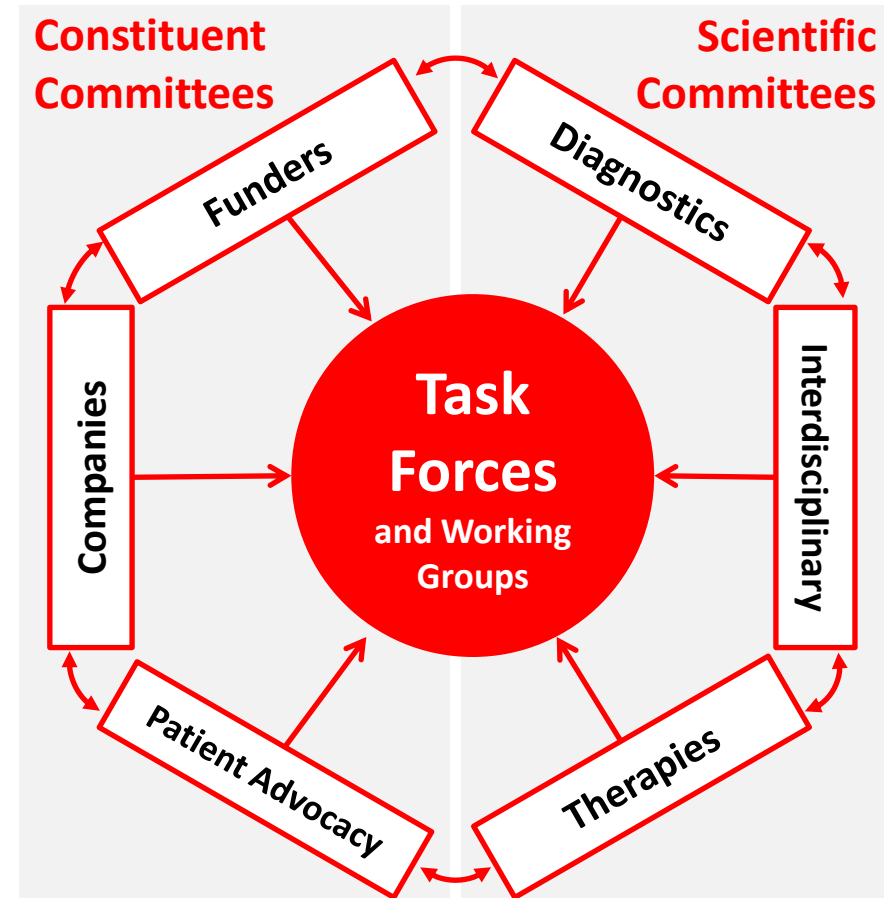
Cumulative number of new orphan drugs since 2010



<https://irdirc.org/research/rd-metrics/>

# Working together towards IRDiRC Goals

- ▶ All Committees propose **priority actions** tackling the three IRDiRC goals
- ▶ **Task Forces** or Working Groups approved by the Consortium Assembly
- ▶ An **annual Road Map** is established by the Assembly
- ▶ Activities are managed by the **Scientific Secretariat**, integrated into the **EJP RD Coordination Office**



Nomination calls for **Task Forces/Working Groups** and **Scientific Committees** published on [www.irdirc.org](http://www.irdirc.org)



# IRDiRC activities - completed

## IRDiRC GOALS

BASIC RESEARCH

PRECLINICAL RESEARCH

CLINICAL RESEARCH

DEVELOPMENT

AUTHORIZATION

ACCESS

## GOAL 1 DIAGNOSIS

▶ Diagnosis beyond genetic analysis

▶ Patient data, privacy and consent

## GOAL 2 THERAPIES

▶ Drug repurposing for RD

▶ Small-population clinical trials  
▶ Patient-centered outcome measures

## GOAL 3 IMPACT

▶ Orphan drug development

▶ Completed

# Tools for the community

## Data sharing and management

### Proposal of a core set of terms to describe human phenotypes by the International Consortium of Human Phenotype Terminologies

#### Introduction

Collectively rare diseases constitute a substantial healthcare burden, although difficult to quantify as most coding nomenclatures do not include specific codes for these diseases. Although each

Nguyen et al. *BMC Medical Ethics* (2019) 20:55  
<https://doi.org/10.1186/s12910-019-0390-x>

BMC Medical Ethics

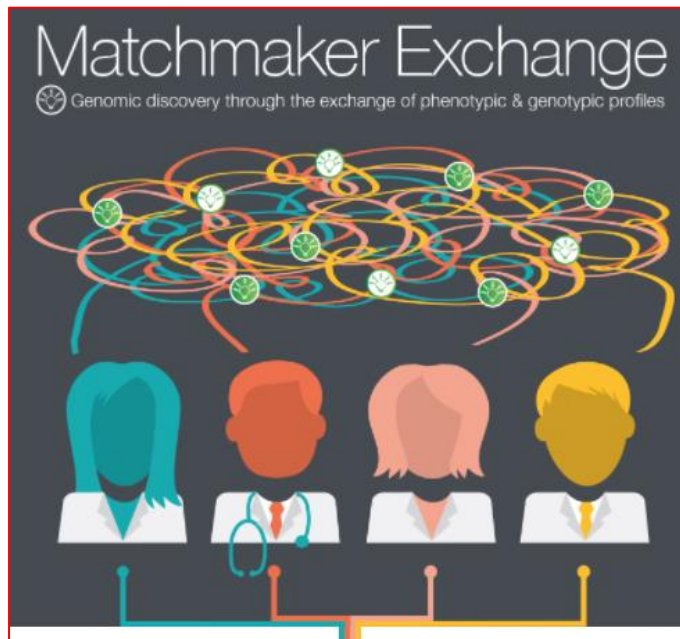
RESEARCH ARTICLE

Open Access

### Model consent clauses for rare disease research



Minh Thu Nguyen<sup>1\*</sup>, Jack Goldblatt<sup>2</sup>, Rosario Isasi<sup>3</sup>, Marlene Jagut<sup>4</sup>, Anneliene Hechtelt Jonker<sup>4</sup>, Petra Kaufmann<sup>5</sup>, Laetitia Ouillade<sup>6</sup>, Fruszina Molnar-Gabor<sup>7</sup>, Mahsa Shabani<sup>8</sup>, Eric Sid<sup>9</sup>, Anne Marie Tassé<sup>1</sup>, Durhane Wong-Rieger<sup>10</sup>, Bartha Maria Knoppers<sup>1</sup> and on behalf of the IRDiRC-GA4GH Model Consent Clauses Task Force



1342

IEEE/ACM TRANSACTIONS ON COMPUTATIONAL BIOLOGY AND BIOINFORMATICS, VOL. 16, NO. 4, JULY/AUGUST 2019

### Privacy-Preserving Linkage of Genomic and Clinical Data Sets

Dixie B. Baker, Bartha M. Knoppers<sup>10</sup>, Mark Phillips<sup>10</sup>, David van Enckevort<sup>10</sup>, Petra Kaufmann, Hanns Lochmuller, and Domenica Taruscio



### Automatable Discovery and Access Matrix ("ADA-M") v1.0

GUIDANCE DOCUMENT

Global Alliance for Genomics & Health (GA4GH)  
International Rare Disease Research Consortium (IRDiRC)

**IRDiRC**

INTERNATIONAL  
RARE DISEASES RESEARCH  
CONSORTIUM

<https://irdirc.org/activities/task-forces/>

# Tools for the community

# Research and innovation

Cell Leading Edge  
Commentary

## A Diagnosis for All Rare Genetic Diseases: The Horizon and the Next Frontiers

Kym M. Boycott,<sup>1,\*</sup> Taila Hartley,<sup>1</sup> Leslie G. Biesecker,<sup>2</sup> Richard A. Gibbs,<sup>3</sup> A. Micheil Innes,<sup>4</sup> Olaf Riess,<sup>5</sup> John Belmont,<sup>6,2</sup> Sally L. Dunwoodie,<sup>7</sup> Nebojsa Jovic,<sup>8</sup> Timo Lassmann,<sup>9</sup> Deborah Mackay,<sup>10</sup> I. Karen Temple,<sup>10</sup> Axel Visel,<sup>11,12,13</sup> and Gareth Baynam<sup>14,15,16</sup>

<sup>1</sup>Children's Hospital of Eastern Ontario Research Institute, University of Ottawa, Ottawa, ON, Canada  
<sup>2</sup>Medical Genomics and Metabolic Genetics Branch, National Human Genome Research Institute, Bethesda, MD, USA  
<sup>3</sup>Human Genome Sequencing Center, Department of Human and Molecular Genetics, Baylor College of Medicine, Houston, TX, USA  
<sup>4</sup>Department of Medical Genetics and Alberta Children's Hospital Research Institute, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada  
<sup>5</sup>Institute of Medical Genetics and Applied Genomics, University of Tübingen, Tübingen, Germany  
<sup>6</sup>Illumina, Madison, WI, USA  
<sup>7</sup>Victor Chang Cardiac Research Institute, Faculty of Medicine, University of New South Wales, Sydney, NSW, Australia  
<sup>8</sup>Microsoft Research, Seattle, Washington, USA  
<sup>9</sup>Telathon Kids Institute, University of Western Australia, Nedlands, WA, Australia  
<sup>10</sup>Department of Human Genetics and Genomic Medicine, Faculty of Medicine, University of Southampton, Southampton, Hampshire, UK  
<sup>11</sup>Environmental Health Sciences Center, University of California, Davis, CA, USA  
<sup>12</sup>DOE Joint Genome Institute, Walnut Creek, CA, USA  
<sup>13</sup>The University of Queensland, St. Lucia, QLD, Australia  
<sup>14</sup>Faculty of Health Sciences, Western Australia, Perth, WA, Australia  
<sup>15</sup>Western Australia, Perth, WA, Australia  
<sup>16</sup>Office of Population Health, Perth, WA, Australia

\*Correspondence: [kboyco@cheo.on.ca](mailto:kboyco@cheo.on.ca)  
<https://doi.org/10.1016/j.cell.2019.08.018>

## INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

### Small Population Clinical Trials Task Force Workshop Report and Recommendations

July 2016

nature reviews drug discovery View all Nature Research journals Search Q Login

Explore our content Journal information Sign up for alerts RSS feed

nature > nature reviews drug discovery > comment > article

COMMENT · 20 APRIL 2020

## Boosting delivery of rare disease therapies: the IRDiRC Orphan Drug Development Guidebook


The International Rare Diseases Research Consortium (IRDiRC) has created a Guidebook to facilitate drug development for rare diseases by organizing available tools into a standardized framework.

Anneliene Hechtelt Jonker, Virginie Hivert, Michela Gabaldo, Liliana Batista, Daniel O'Connor, Annelieke Aartsma-Rus, Simon Day, Ken Sakushima & Diego Ardigo

Southall et al. *Orphanet Journal of Rare Diseases* (2019) 14:225  
<https://doi.org/10.1186/s13023-019-1193-3>

Orphanet Journal of Rare Diseases

**POSITION STATEMENT** Open Access



## The use or generation of biomedical data and existing medicines to discover and establish new treatments for patients with rare diseases – recommendations of the IRDiRC Data Mining and Repurposing Task Force

Noel T Southall<sup>1\*</sup>, Madhusudan Natarajan<sup>2</sup>, Lilian Pek Lian Lau<sup>1,3</sup>, Anneliene Hechtelt Jonker<sup>3</sup>, Benoît Deprez<sup>4,5</sup>, Tim Guillems<sup>6</sup>, Lawrence Hunter<sup>7</sup>, Carin MA Rademaker<sup>8</sup>, Virginie Hivert<sup>9</sup>, Diego Ardigo<sup>10</sup> and on behalf of the IRDiRC Data Mining and Repurposing Task Force

[Orphanet J Rare Dis. 2017; 12: 171.](https://doi.org/10.1186/s13023-017-0718-x) PMCID: PMC5667521  
 Published online 2017 Nov 2. doi: [10.1186/s13023-017-0718-x](https://doi.org/10.1186/s13023-017-0718-x) PMID: [29096663](https://pubmed.ncbi.nlm.nih.gov/29096663/)

## Measuring what matters to rare disease patients – reflections on the work by the IRDiRC taskforce on patient-centered outcome measures

[Thomas More](#)<sup>1</sup> and [Stefan J. Cano](#)<sup>2</sup>



# IRDiRC ongoing/new activities

## Research and development for RD

### IRDiRC GOALS

BASIC RESEARCH

PRECLINICAL RESEARCH

CLINICAL RESEARCH

DEVELOPMENT

AUTHORIZATION

ACCESS

### GOAL 1 DIAGNOSIS

▶ Implementing new diagnostic tools

▶ Disregarded rare diseases

### GOAL 2 THERAPIES

▶ Making RD research attractive to industry

▶ Drug repurposing for RD

### GOAL 3 IMPACT

▶ Ongoing



**IRDiRC**  
INTERNATIONAL  
RARE DISEASES RESEARCH  
CONSORTIUM

<https://irdirc.org/activities/task-forces/>

# IRDiRC ongoing /new activities

## Innovation in clinical RD research

### IRDiRC GOALS

#### GOAL 1 DIAGNOSIS

#### GOAL 2 THERAPIES

#### GOAL 3 IMPACT



▶ Leveraging the existing clinical ecosystem

▶ Widening patient access to clinical trials

▶ Medical devices for RD

▶ Ongoing

▶ New

# IRDiRC ongoing /new activities

## Access and impact

IRDiRC GOALS

BASIC RESEARCH

PRECLINICAL RESEARCH

CLINICAL RESEARCH

DEVELOPMENT

AUTHORIZATION

ACCESS

GOAL 1  
DIAGNOSIS

GOAL 2  
THERAPIES

GOAL 3  
IMPACT

▶ Diagnosis for Indigenous populations

▶ Tele-medicine

▶ Primary care

▶ Access barriers to therapies

▶ Impact of diagnosis and therapies on peoples lives

▶ Ongoing

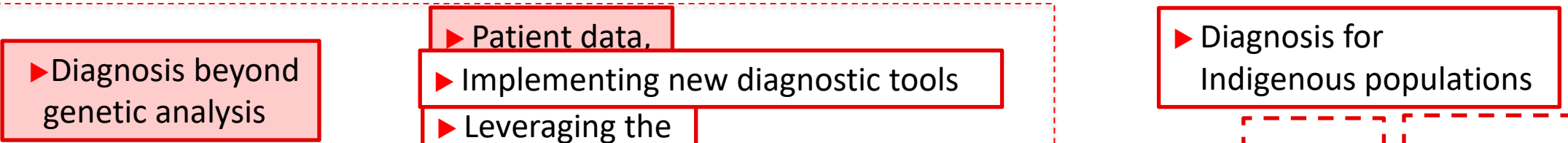
▶ New

# IRDiRC's widening horizons

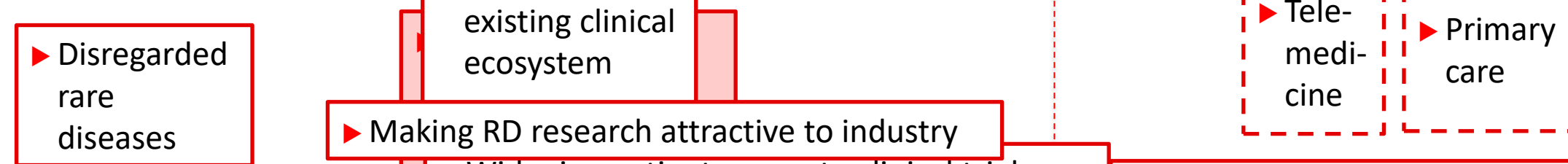
## IRDiRC GOALS



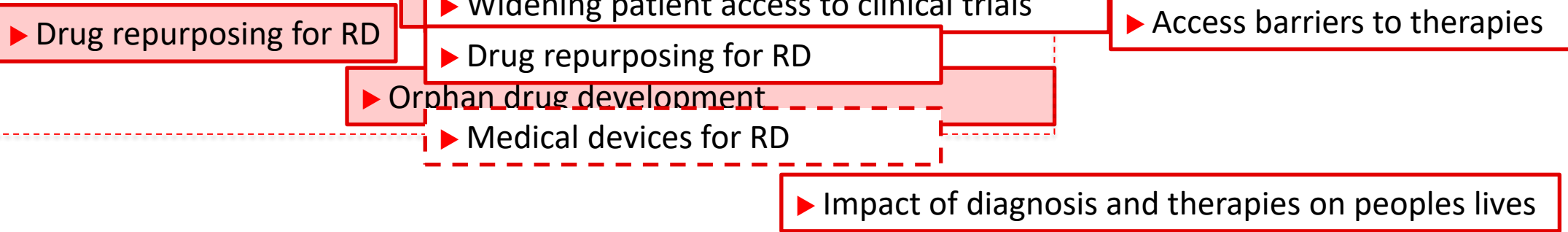
### GOAL 1 DIAGNOSIS



### GOAL 2 THERAPIES



### GOAL 3 IMPACT



- ▶ Completed
- ▶ Ongoing
- ▶ New



<https://irdirc.org/activities/task-forces/>



# THANK YOU!

<https://irdirc.org/>



Funded by the  
European Union  
GA N°825575



**IRDiRC**  
INTERNATIONAL  
RARE DISEASES RESEARCH  
CONSORTIUM

IRDiRC Consortium Assembly meeting  
Paris, 21-22 November 2019