Participant Involvement: USA

International Rare Disease Research Consortium
08 November 2014

Sharon F. Terry
President & CEO, Genetic Alliance
Founding CEO, PXE International
President, EspeRare
Principal Investigator, CENA

Why are we here?

An **ecosystem** is a community of living organisms (plants, animals and microbes) in conjunction with the nonliving components of their environment (things like air, water and mineral soil), interacting as a system. These components are regarded as linked together through nutrient cycles and energy flows

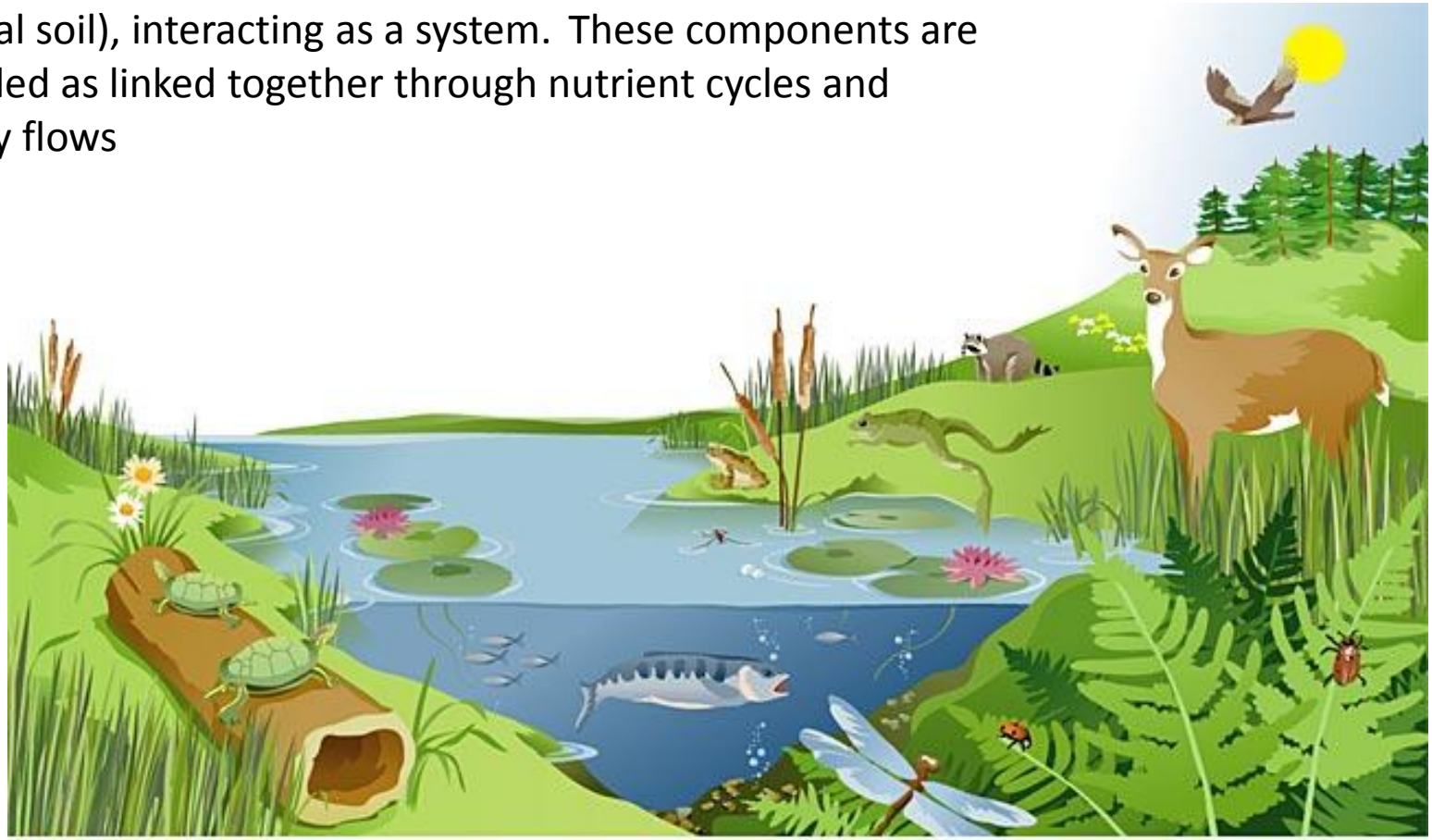


illustration by Jeff Grader / property of Delta Education

Why are we here?

A drug development **ecosystem** is a community of stakeholders (universities, companies, patient organizations, patients, government organizations) in conjunction with the nonliving components of their environment (things like regulations, economic factors, reimbursement potential), interacting as a system. These components are regarded as linked together through clinical research cycles and funding flows

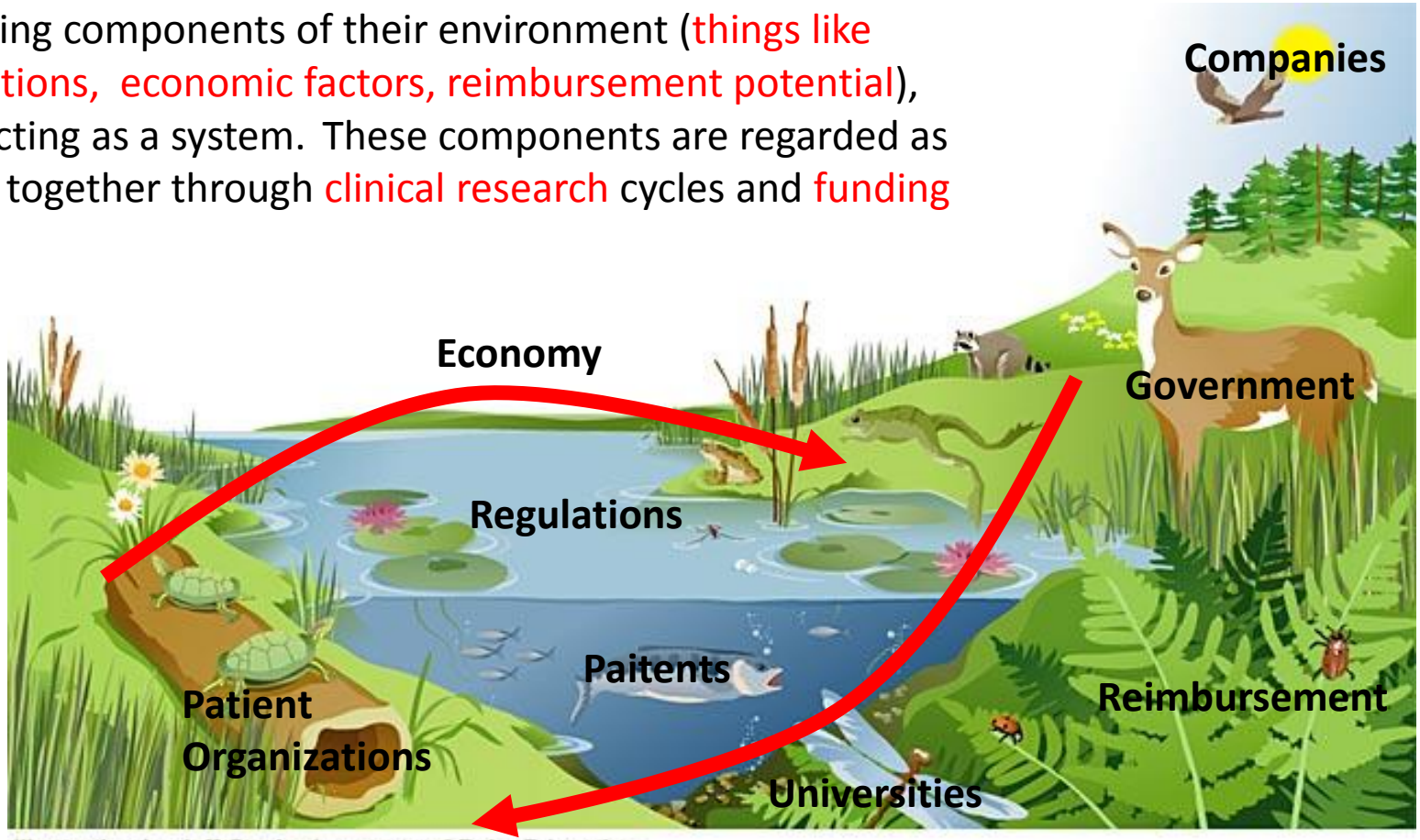


illustration by Jeff Grader / property of Delta Education

Challenges in Rare Genetic Disease Research

- Limited participants
- Variable disease phenotyping
- Limited bio- sample & data repositories
- Fragmentation / lack of scale
- Limited privacy & data security
- Limited funding → limited research
- Poor feedback to participants

There is no deli number…

Our Approach

Create a Commodity to:

- Organize a Community
- Leverage & Offer Funding
- Coordinate Research & Studies
- Coordinate Communications
- Focus on Clinical Significance

Elizabeth and Ian diagnosed with pseudoxanthoma elasticum (PXE)

1994

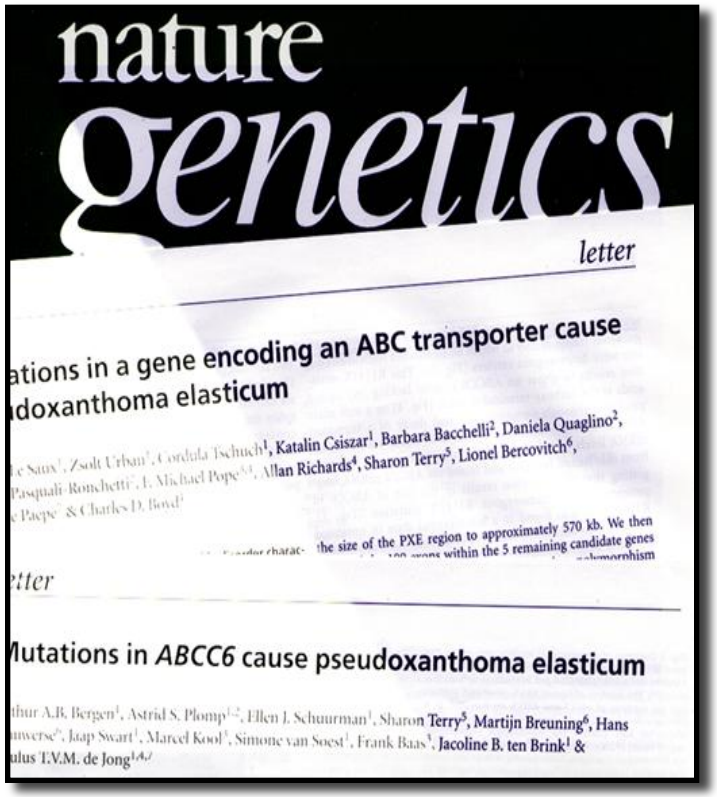
2014

Elizabeth:
Teach for America

Ian:
Organic Farmer

PXE international

Gene Discovery



nature genetics

letter

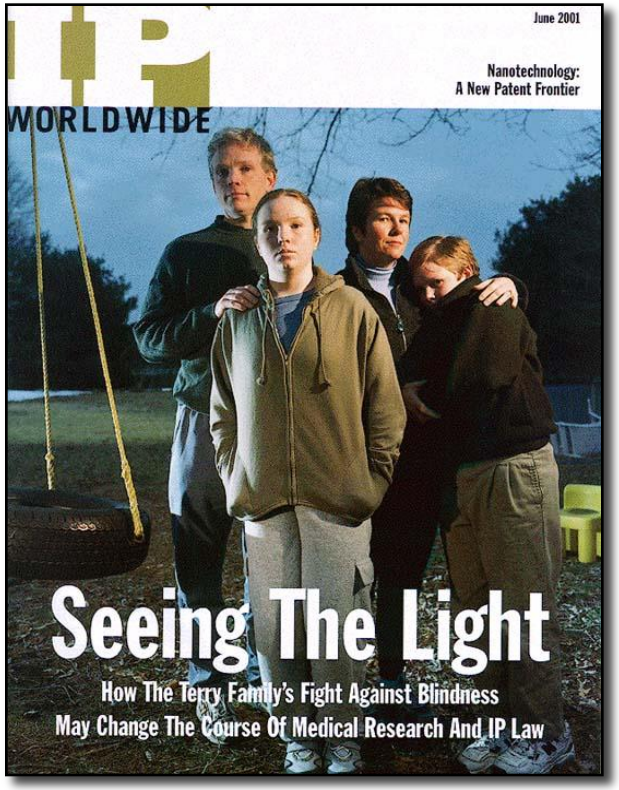
ations in a gene encoding an ABC transporter cause
doxanthoma elasticum

Mutations in *ABCC6* cause pseudoxanthoma elasticum

BioBank

Testing

Clinical
Diagnostic
Test
Development
via FDA & CLIA
Regulatory
Strategies



Patenting

Licensing & Intellectual Property Management

Human Clinical Trials

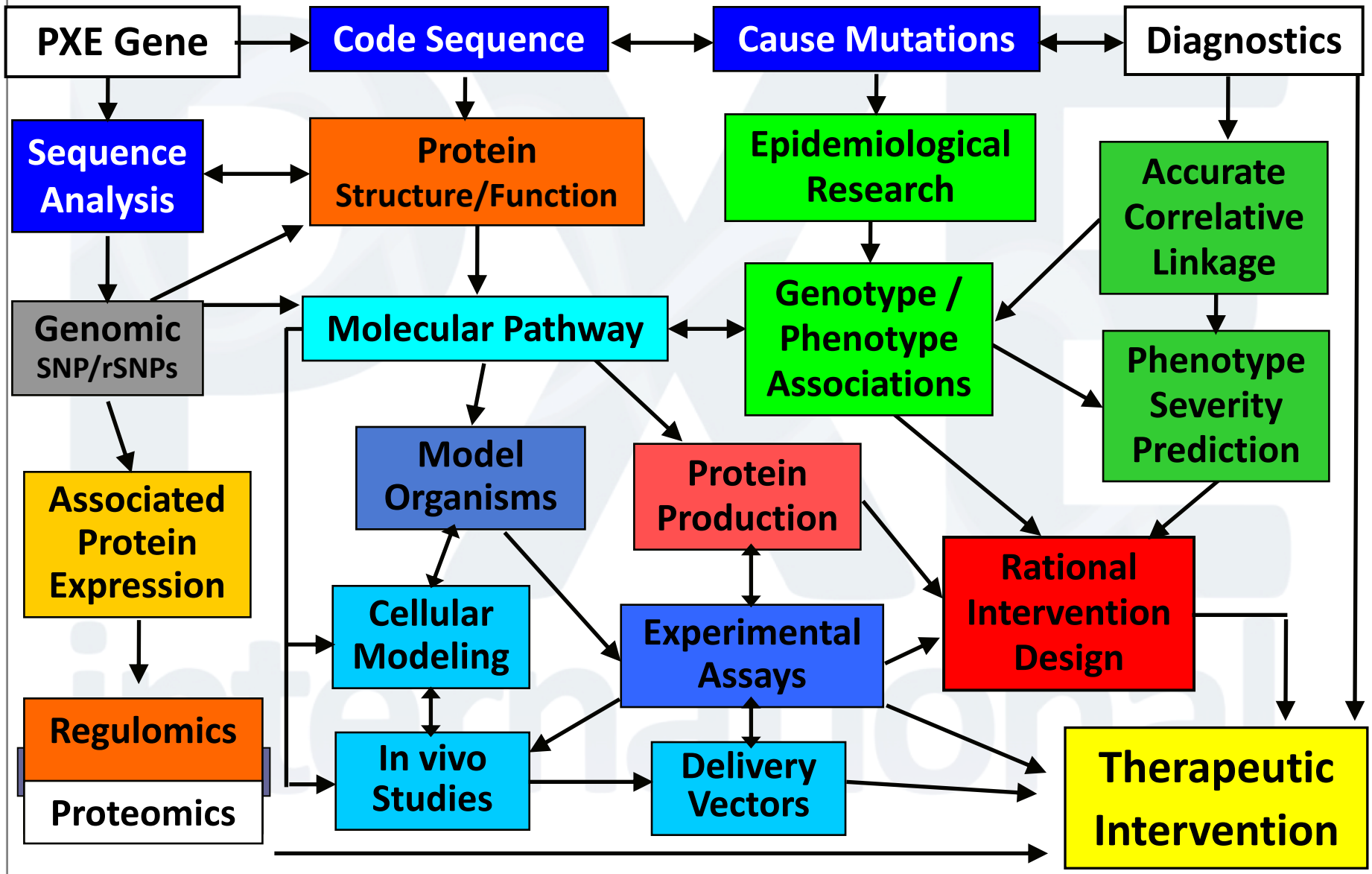
Drug Screening & Development Approaches

Therapeutics

--Small Molecules

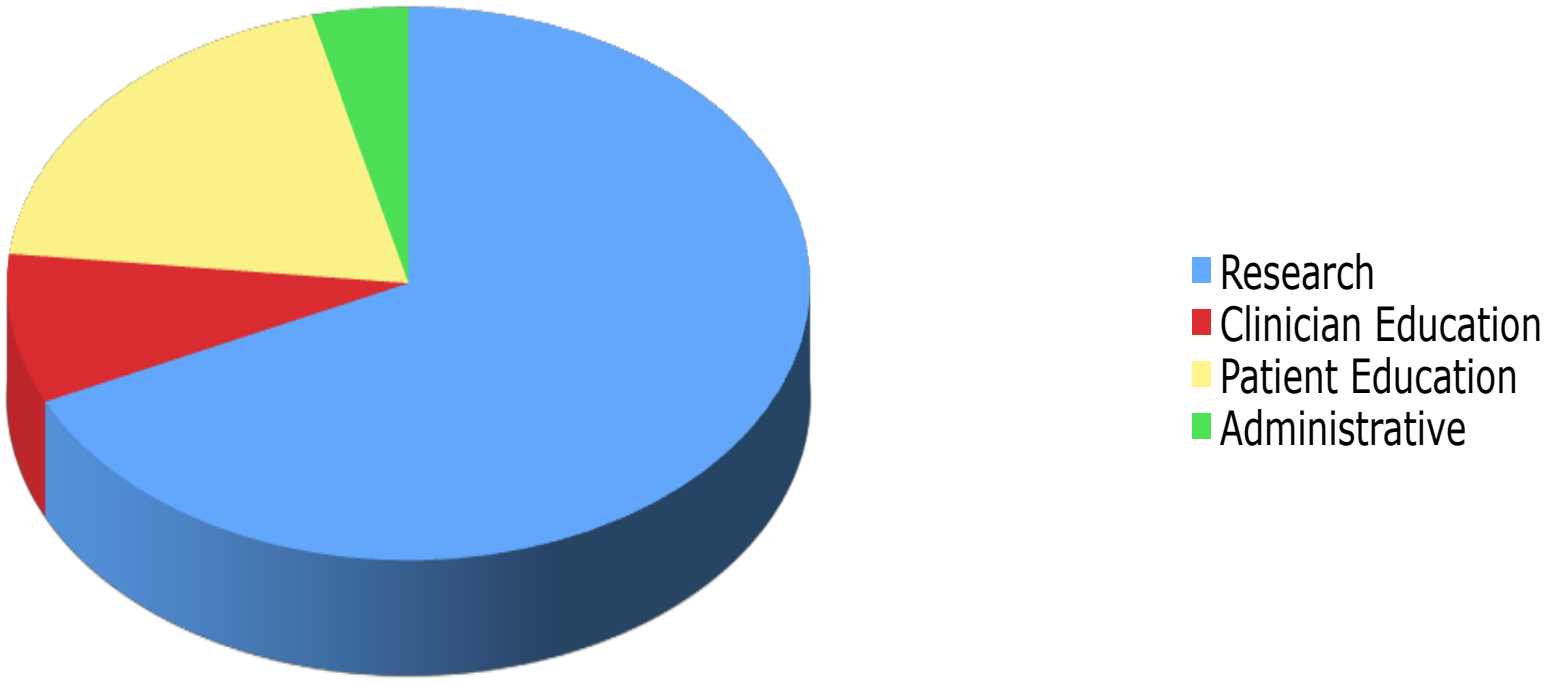
--Nonsense mutants

20 Years Into Project Plan



PXE international

Spending



- 1995 Incorporation
- Nonprofit Advocacy Foundation
- Raised/Invested ~$2,800,000
- Leveraged ~$19,000,000 Federal Funds
- Gene & Diagnostic Patents
- Animal Model
- Clinical Genetic Testing
- Human Clinical Intervention Trials
- Drug Discovery Screening Program

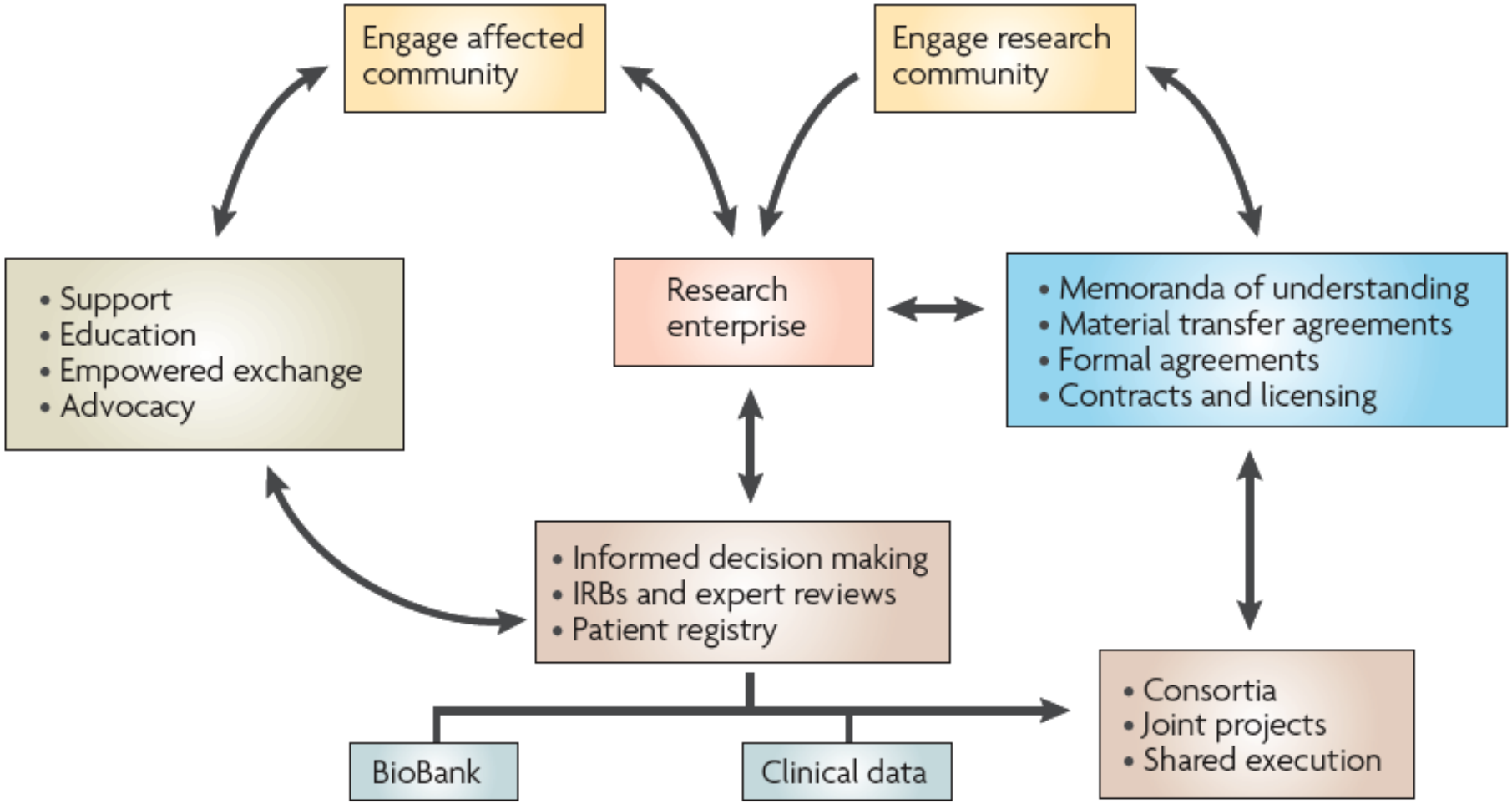


Figure 1 | **The PXE International strategy.** PXE International uses a variety of approaches to bring the PXE community together with research scientists to accelerate translational research. IRB, institutional review board.

Terry SF, Terry PF, Rauen K, Uitto J, Bercovitch L. Advocacy Organizations as Research Organizations: the PXE International example. Nature Reviews Genetics. 2007 Feb; Vol. 8, No. 2

PXE international

PXE: Taming the disease through industrialized translational research - scale, focus and collaboration.

PXE International Consortium:

- Research Management
- Secure Informatics Infrastructure
- Genomic Sample & Data Bank
- Collaborative Research Projects
  - Correlative Science
  - FDA Diagnostic Kit
- Scientific & Commercial Partnerships

BRC

Thomas Jefferson University | Jefferson Medical College

TRANSGENOMIC®
transforming the world

BROWN UNIVERSITY

UNIVERSITEIT GENT

National Human Genome Research Institute

Pediatric Symposium:
Focus on Pediatric Rare Diseases

November 6, 2014

Audrey Gordon, Esq.
President, Executive Director - The Progeria Research Foundation

PRF-Identified Cases Reside In 43 Countries

Argentina	Chile	Dominican Republic	Guatemala	Israel	Namibia	Poland	Spain	Turkey
Australia	China	Egypt	Honduras	Italy	Nepal	Portugal	Sweden	USA
Belgium	Colombia	England	India	Japan	Pakistan	Russia	Tajikistan	Venezuela
Brazil	Czech Republic	France	Indonesia	Libya	Peru	South Africa	Tanzania	
Canada	Denmark	Germany	Ireland	Mexico	Philippines	South Korea	Togo	

Progeria Research Foundation

…and Speak 28 Languages

Arabic	English	Indonesian	Marathi	Swahili	Turkish
Chinese	French	Italian	Polish	Swedish	Urdu
Czech	German	Japanese	Portuguese	Tagalog	Uzbek
Danish	Hebrew	Kannada	Russian	Tajik	
Dutch	Hindi	Korean	Spanish	Telugu	

బాలుడ బాలిక వయస్స ముదరుకండానే వృద్ధాప్యరూపంలోనికి వచ్చుట రీసెర్చ్ ఫౌండేషన్

مؤسسة أبحاث الشيخ

早衰症研究基金會

Progeria रिसरच फाउंडेशन

早老症研究財団

조로증 연구 재단

Progeria Araştırma Vakfı

прогерии исследовательский фонд

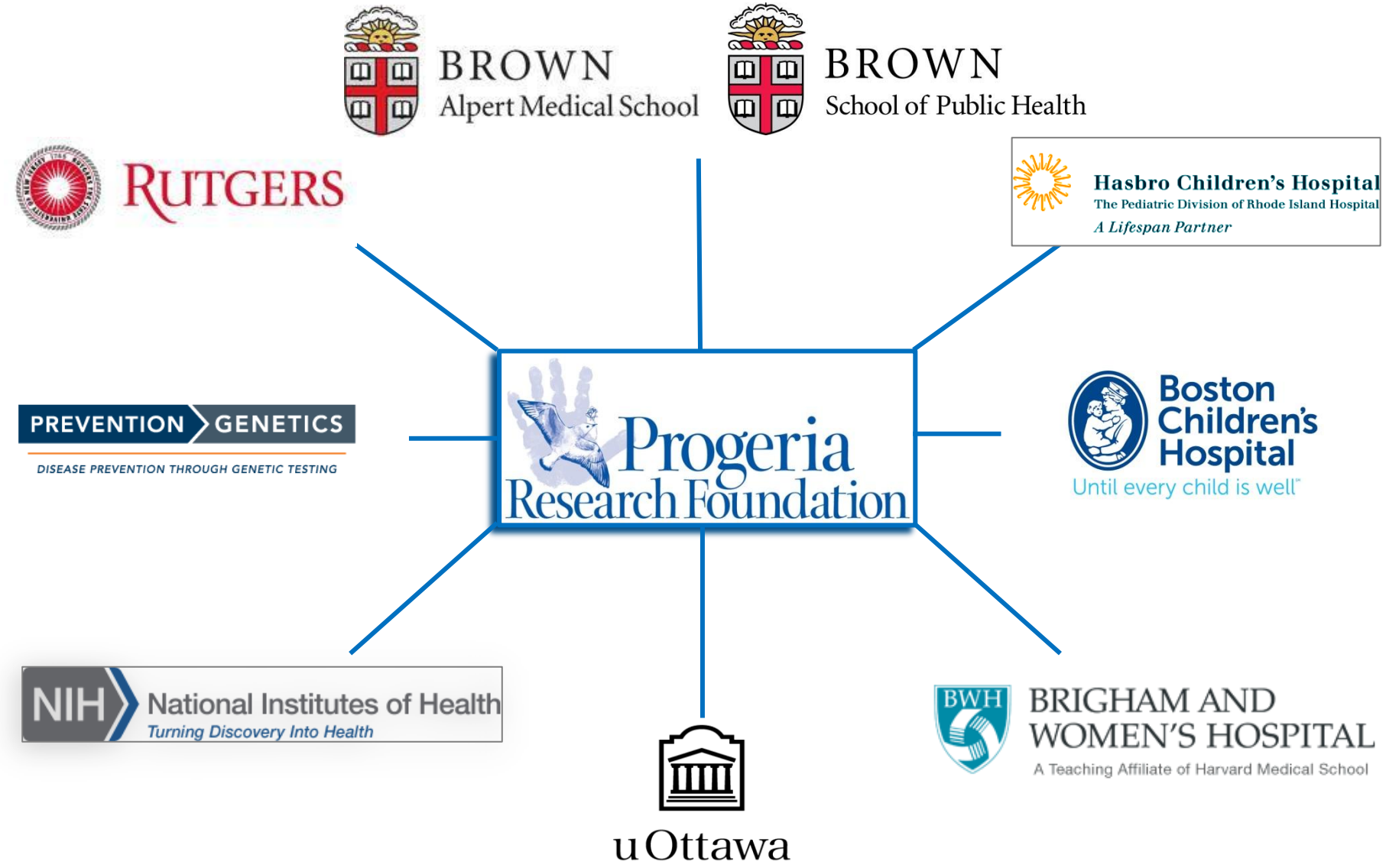
Progeria Research Foundation

Our History, Our Future…

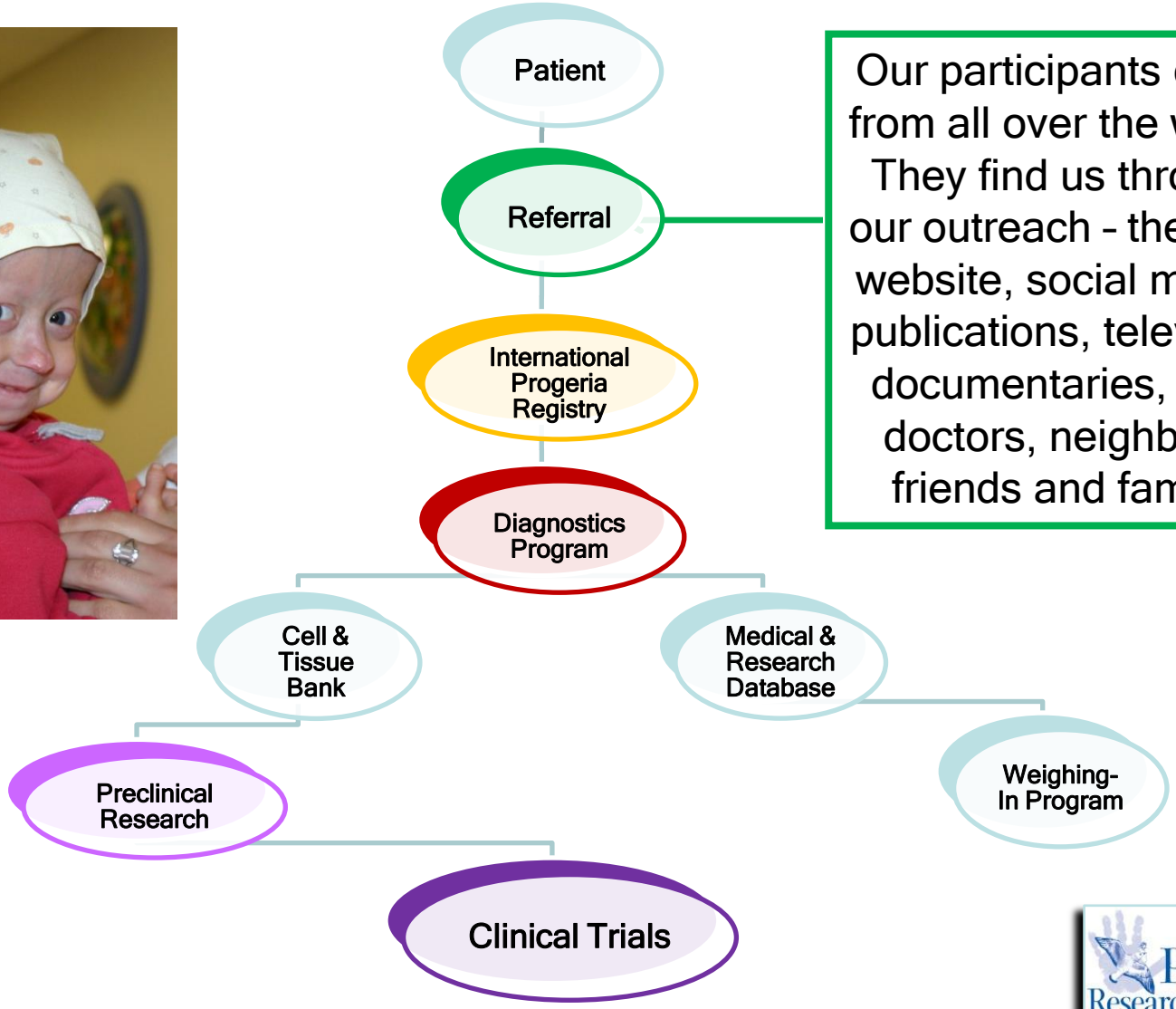
- 1999: No research, No awareness, No knowledge
- 2003: Gene Discovery – The doors of science are flung open
- 2007: First Trial – A drug is identified as a potential treatment
- 2012: First Treatment – Trial results show the drug benefits children‘s cardiovascular status
- 2014: Longer Life - Time reveals the first treatment shows increased estimated lifespan
- ONGOING: Discovering better treatments and a cure

Progeria Research Foundation

PRF Programs: Collaborations For Success



PRF Programs: It All Starts With The Children



Our participants come from all over the world. They find us through our outreach – the PRF website, social media, publications, television documentaries, their doctors, neighbors, friends and family.

Progeria Research Foundation

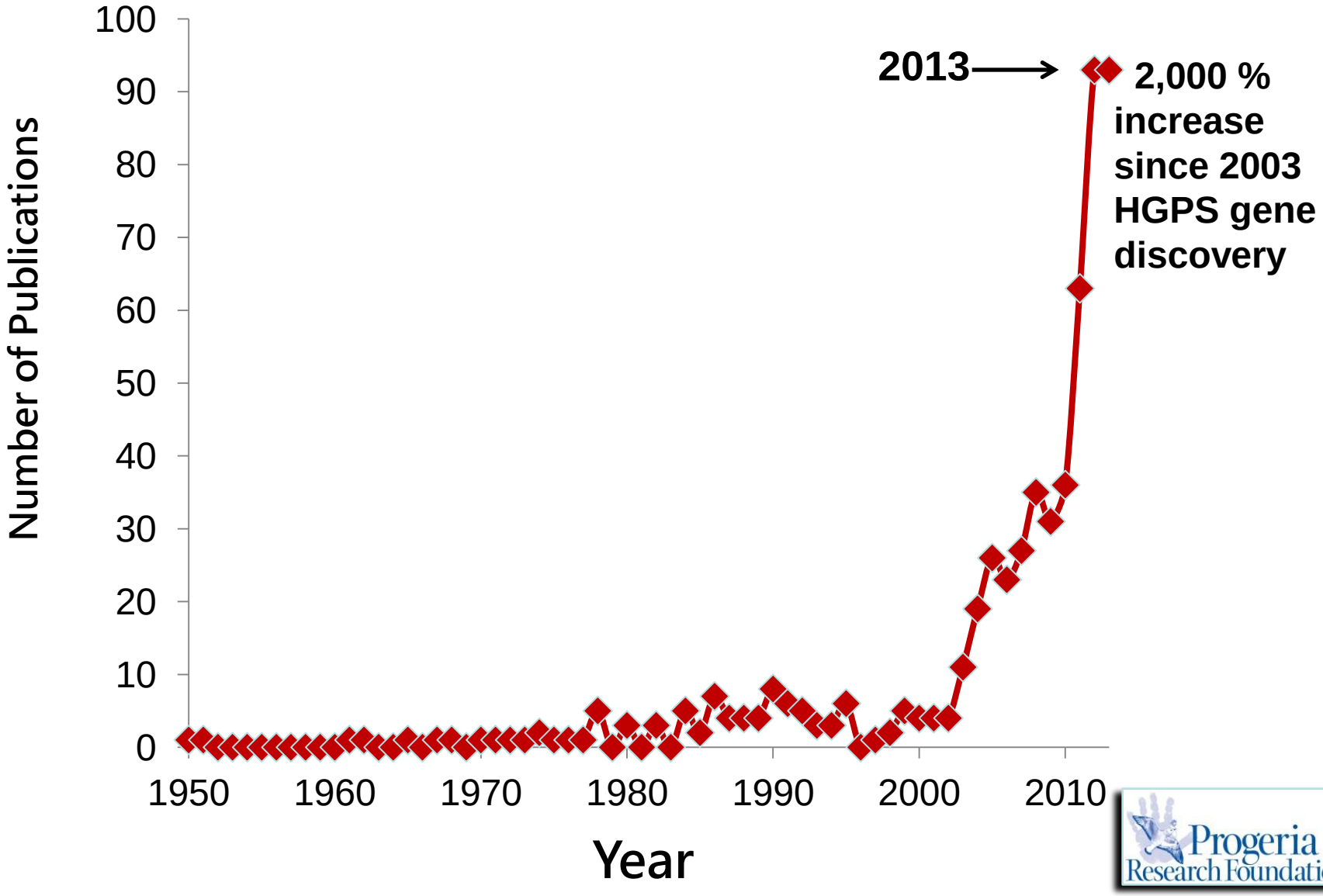
Growth of Global Interest in Progeria Research

Research Grants:
54 projects ($6 million) to
51 researchers in **10** countries

Scientific Workshops:
11 International conferences (30-40% participation increase)

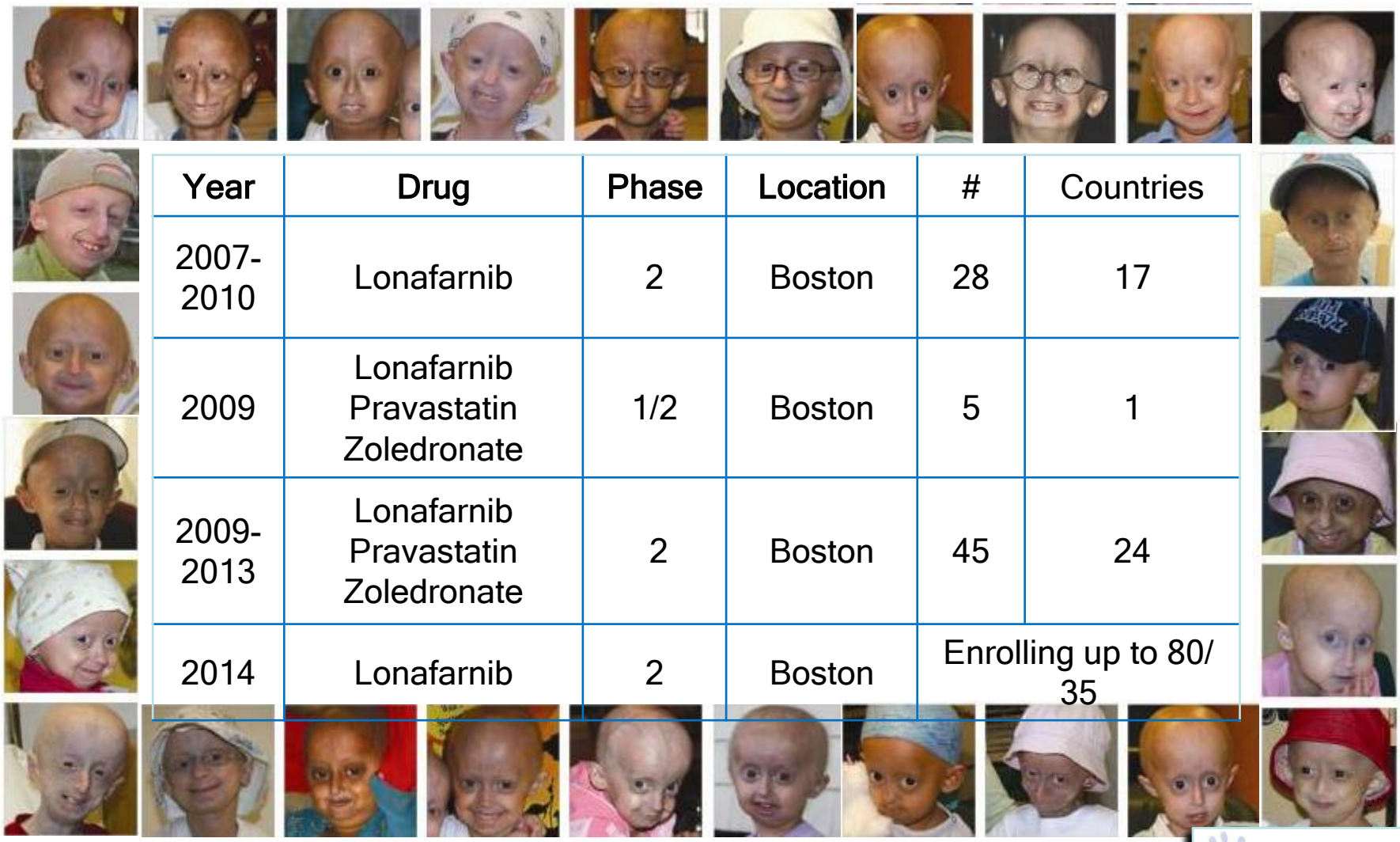
Progeria Research Foundation

Progeria Publications Trend



Progeria Research Foundation

PRF -Funded Clinical Treatment Trials



Year	Drug	Phase	Location	#	Countries
2007-2010	Lonafarnib	2	Boston	28	17
2009	Lonafarnib Pravastatin Zoledronate	1/2	Boston	5	1
2009-2013	Lonafarnib Pravastatin Zoledronate	2	Boston	45	24
2014	Lonafarnib	2	Boston	Enrolling up to 80/35	

Progeria Research Foundation

Clinical Treatment Trial Publications

As of October 1, 2014:

- **Dermatology:** Initial Cutaneous Manifestations of Hutchinson-Gilford Progeria Syndrome – *Pediatric Dermatology*, 2014,1-7.
- **Drug Effect:** Neurologic Features of Hutchinson-Gilford Progeria Syndrome after Lonafarnib Treatment – *Neurology*, 2013, 81:427-430.
- **Drug Effect:**, Clinical Trial of a Farnesyltransferase Inhibitor in Children with Hutchinson-Gilford Progeria Syndrome, Gordon et al, *Proceedings of the National Academy of Sciences*, 2012 Sep 24.
- **X-ray:** A Prospective Study of Radiographic Manifestations in Hutchinson-Gilford Progeria Syndrome, Cleveland et al,, *Pediatric Radiology,* 2012 Sep;42(9):1089-98. Epub 2012 Jul 1.
- **Cardiology:** Mechanisms of Premature Vascular Aging in Children with Hutchinson-Gilford Progeria Syndrome. Gerhard-Herman M, et al., *Hypertension*. 2012 Jan;59(1):92-97; Epub 2011 Nov 14.
- **Skeleton:** Hutchinson-Gilford progeria is a skeletal dysplasia. Gordon,et al., *J Bone Miner Res*. 2011 Jul;26(7):1670-9.

Progeria Research Foundation

CPAG
Coalition of Patient Advocacy Groups

Collectively, the Coalition of Patient Advocacy Groups (CPAG) represents the perspective and interests of all patient advocacy organizations associated with the clinical research consortia. Through collaboration, patient advocacy groups and researchers can make faster progress toward new treatment options and cures, which can improve the lives of all persons and families affected by a rare disease. Learn More > | CPAG Committee Roster

News

Featured Links

- NORD
- NIH Office of Rare Diseases
- Genetic and Rare Diseases Information Center (GARD)
- Genetic Alliance
- AARDA
- OOPD/FDA

Rare Diseases Advocacy Groups

Click on a Rare Diseases Network Consortium to see corresponding advocacy groups:

- Angelman, Rett, and Prader-Willi Syndromes Consortium
- Autonomic Rare Diseases Clinical Research Consortium
- Brain Vascular Malformation Consortium
- Chronic Graft Versus Host Disease Consortium (cGVHD)
- Dystonia Coalition
- Genetic Disorders of Mucociliary Clearance Consortium
- Inherited Neuropathies Consortium
- LDN Lysosomal Disease Network
- NEPTUNE: Nephrotic Syndrome Rare Disease Clinical Research Network
- North American Mitochondrial Diseases Consortium
- Porphyrias Consortium
- Primary Immune Deficiency Treatment Consortium (PIDTC)
- Rare Kidney Stone Consortium
- Salivary Gland Carcinomas Consortium
- STAIR: Sterol and Isoprenoid Diseases Consortium
- Urea Cycle Disorders Consortium
- Vasculitis Clinical Research Consortium

pcornet
The National Patient-Centered Clinical Research Network

Patient Powered Research Networks

Organization	PI	Condition	Proposed PPRN Population Size
Accelerated Cure Project for Multiple Sclerosis	Robert McBurney	Multiple Sclerosis	20,000
American Sleep Apnea Association	Susan Redline	Sleep Apnea	50,000
Cincinnati Children's Hospital Medical Center	Peter Margolis	Pediatric Crohn's Disease and Ulcerative Colitis	15,000
COPD Foundation	Richard Mularski	Chronic Obstructive Pulmonary Disease	50,000
Crohn's and Colitis Foundation of America	R. Balfour Sartor	Inflammatory Bowel Disease (Crohn's disease and ulcerative colitis)	30,000
Global Healthy Living Foundation	Seth Ginsberg	Arthritis (rheumatoid arthritis, spondyloarthritis), musculoskeletal disorders (osteoporosis), and inflammatory conditions (psoriasis)	50,000
Massachusetts General Hospital	Andrew Nierenberg	Major Depressive Disorder (MDD) and Bipolar Disorder (BP)	50,000
Univ of California, San Francisco	Mark Pletcher	Cardiovascular health	100,000
University of South Florida	Rebecca Sutphen	Hereditary Breast and Ovarian Cancer (HBOC)	17,000

….in both rare and common disorders

Organization	PI	Condition	Proposed PPRN Population Size
ALD Connect, Inc	Florian Eichler	Adrenoleukodystrophy	3,000
Arbor Research Collaborative for Health	Bruce Robinson	Primary Nephrotic Syndrome (Focal Segmental Glomerulosclerosis [FSGS], Minimal Change Disease [MCD], and Membranous Nephropathy [MN] Multiple Sclerosis	1,250
Duke University	Laura Schanberg	Juvenile Rheumatic Disease	9,000
Epilepsy Foundation	Janice Beulow	Aicardi Syndrome, Lennox-Gastaut Syndrome, Phelan-McDermid Syndrome, Hypothalamic Hamartoma, Dravet Syndrome, and Tuberous Sclerosis	1,500
Genetic Alliance, Inc	Sharon Terry	Alström syndrome , Dyskeratosis congenital, Gaucher disease, Hepatitis, Inflammatory breast cancer, Joubert syndrome, Klinefelter syndrome and associated conditions, Metachromatic leukodystrophy, Pseudoxanthoma elasticum (PXE)	50- 50,000
Immune Deficiency Foundation	Kathleen Sullivan	Primary Immunodeficiency Diseases	1,250
Parent Project Muscular Dystrophy	Holly Peay	Duchenne and Becker muscular dystrophy	4,000
Phelan-McDermid Syndrome Foundation	Megan O'Boyle	Phelan-McDermid Syndrome	737
University of Pennsylvania	Peter Merkel	Vasculitis	500

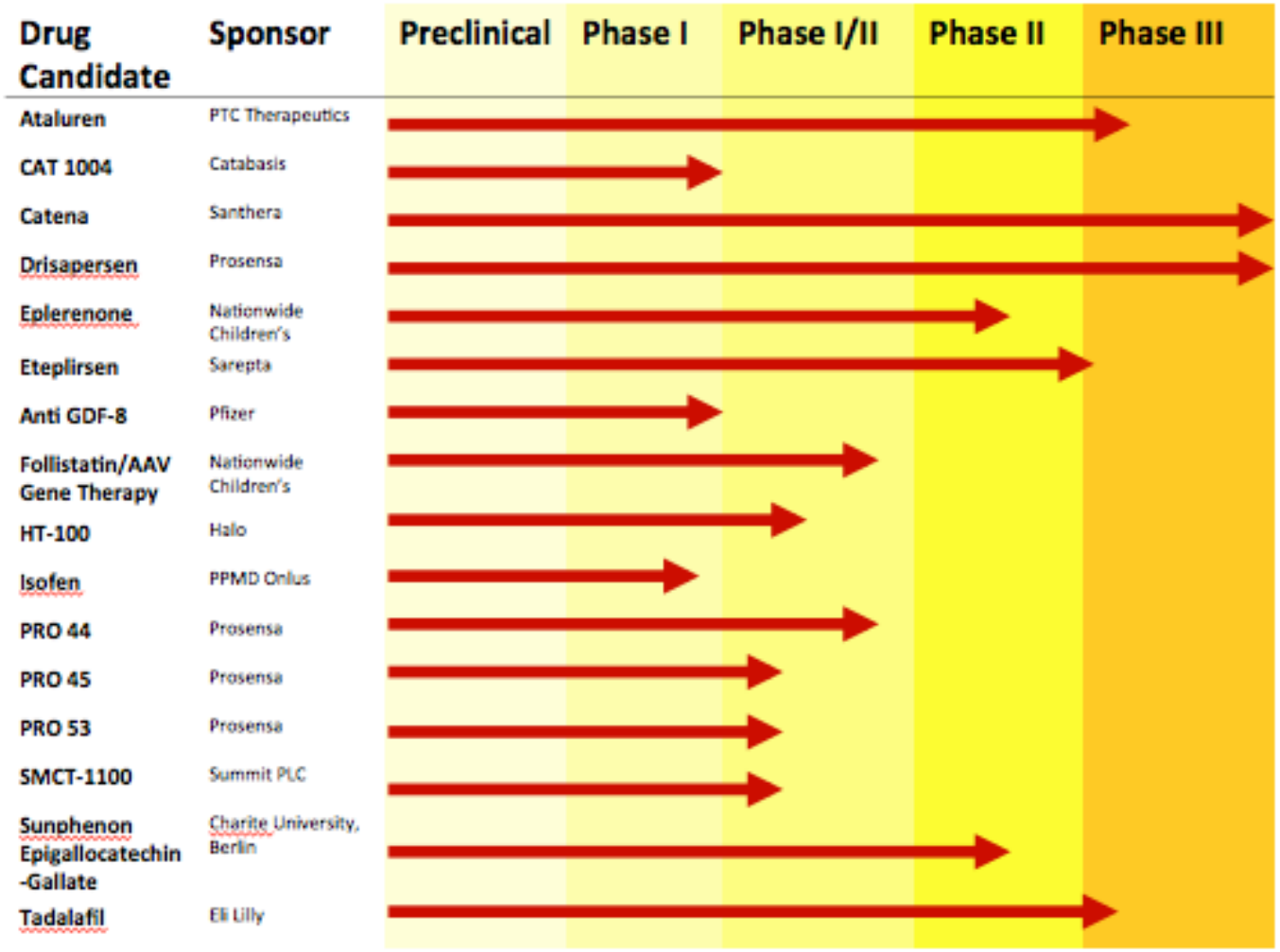
Parent Project Muscular Dystrophy

Leading the Duchenne muscular dystrophy community

Our Mission:

To improve the treatment, quality of life and long-term outlook for all individuals affected by Duchenne muscular dystrophy through research, education, advocacy and compassion.

A Drug Development Pipeline in Duchenne Full of Potential



DMD caregiver study

- To promote **patient-centered drug development** in the area of DMD, PPMD conducted a national survey caregivers of a child with DMD.

- To quantify **treatment preferences** of caregivers of a child with DMD for the potential benefits and risk of potential treatments we utilize a cutting edge stated-preference method: Best-Worst Scaling (BWS)

- In our BWS experiment, we presented caregivers with **potential treatments** (profiles) and asked them to select the best and worst features.

- Features included **benefits, risk and other characteristics** of potential treatments

Community-centered research

- PPMD led the study, guided by an **advocacy oversight team** comprising PPMD staff members who collaborated with the **research team** to design and implement the study.

- The broader DMD community was engaged to develop the survey (clinicians, sponsors, families).

- The oversight team made **study-related decisions** through a consensus process.

- Contributing authors included **PPMD staff** and academic collaborators from **Johns Hopkins**.

Treatment preferences

- A pool of **treatment features** (attributes) identified and refined in consultation with parents, clinicians, and industry

- **Six attributes** were chosen to cover the potential benefits, risks and other features, each varying across **three levels** each.

- A main-effects orthogonal array was used as the basis of the **experimental design** - identifying 18 potential treatments that systematically varied across the six chosen attributes.

Attributes and levels

- **Effect on muscle function** (none, slows, stops)
- **Gain in expected lifespan** (none, 2, 5 years)
- **Post-approval information** (none, 1, 2 years)
- **Nausea** (none, loss of appetite, loss of appetite and occasional vomiting)
- **Risk of bleeds** (none, risk of bleeding gums and increased bruising, risk of hemorrhagic stroke)
- **Risk of heart arrhythmia** (none, risk of harmless heart arrhythmia, risk of dangerous heart arrhythmia and sudden death)

Conclusions – Treatment priorities

- Within the context our preference experiment:
  - Stopping/slowing the **progression of muscle weakness** accounted for the largest proportion of the variation.
  - The presence of a serious **risk** could be compensated for by a treatment that stops/slows progression to muscle function.
  - **Nausea** was viewed negatively, but not nearly as negatively as a risk for a serious health event.
  - Caregivers *marginally* valued **post-market data**

Genetic Alliance Registry & BioBank

Advocacy owned and managed data repository and samples

Clinical Information Medical Records

DNA/RNA Self-reported Data

Cell Lines Tissue / Organs

30,000 samples + 20,000 clinical records

BioBank.org

Genetic Alliance Registry and BioBank Toolbox

Where do I begin?	What is a biobank?	Guidelines for considering a registry/biobank	Advocates are leaders in biobanking	
How do I make this a reality?	Registry/ repository start-up guide	Making your organization's biobank a reality	Genetic Alliance registry/repository boot camps	
Is my organization ready?	Organizational readiness checklist	Biobank question & answer session		
How do I select a vendor?	Vendor assessment summary	Vendor assessment worksheet	Landscape analysis manuscript	
Considering Genetic Alliance?	Genetic Alliance BioBank	GARB FAQs	Virtual tour of Genetic Alliance registry solutions	GARB history manuscript
What else do I need to know?	Biobank governance	Biobank governance checklist	Resource list	
How do I stay current?	Registry and Biorepository Bulletin	BioBank discussion listserv	BioBank Ambassadors mentoring	Weekly tips

Publication *Training/mentoring* *Videos* *Webinar* *Webpage* *Worksheet*

White label registry – branded according to the advocacy organizations wishes

The portal fits directly onto any web page and retains the host site's top and bottom navigation

home about us scientific info conference events news shop donate join us member login contact us

Joubert Syndrome & Related Disorders Foundation

Together we can advance research and improve care

For over 22 years, JSRDF has played an important role in educating physicians and their support teams as well as increasing public awareness about Joubert syndrome. The goal of JS-LIFE (Joubert Syndrome Link to Information & Family Exchange) is to extend this tradition of leadership by enabling access to a much broader research community of clinical, neuroimaging, and genetic studies. This information will help us discover patterns within the data collected and bridge the gap in knowledge that exists among other related disorders and ciliopathy researchers. Please join us. Simply click on Start Now! to begin, or Sign In if you are a returning user.

Support | Educate | Research

Joubert Syndrome Link to Information & Family Exchange

Privacy and Sharing in Perfect Balance

To help us protect your individual privacy in accordance with rules that you establish, we harness the power of Private Access with the specific goal of helping you make your health information available to top researchers - under your own terms.

PRIVACY ASSURED

It's quick and simple!

1. Sign up! (or sign in) Start Now!
2. Take a health survey
3. Let researchers find you
4. Share this with others!

MY DOCTOR OR DISEASE ADVOCACY GROUP RECOMMENDED THIS SERVICE AND PROVIDED ME WITH A REFERRAL #:

Enter referral # here Submit

Privacy Policy Terms of Service Give Feedback

© 2013-2014 Genetic Alliance, Inc. All rights reserved

White label registry – branded according to the advocacy organizations wishes

The portal fits directly onto any web page and retains the host site's top and bottom navigation

The headline, colors, theme, video and other content can be tailored to fit seamlessly into the host site and support each group's message.

home about us scientific info conference events news shop donate join us member login contact us

Joubert Syndrome & Related Disorders Foundation

Together we can advance research and improve care

For over 22 years, JSRDF has played an important role in educating physicians and their support teams as well as increasing public awareness about Joubert syndrome. The goal of JS-LIFE (Joubert Syndrome Link to Information & Family Exchange) is to extend this tradition of leadership by enabling access to a much broader research community of clinical, neuroimaging, and genetic studies. This information will help us discover patterns within the data collected and bridge the gap in knowledge that exists among other related disorders and ciliopathy researchers. Please join us. Simply click on Start Now! to begin, or Sign In if you are a returning user.

Support | Educate | Research

Joubert Syndrome Link to Information & Family Exchange

It's quick and simple!

1. Sign up! (or sign in) Start Now!
2. Take a health survey
3. Let researchers find you
4. Share this with others!

Privacy and Sharing in Perfect Balance

To help us protect your individual privacy in accordance with rules that you establish, we harness the power of Private Access with the specific goal of helping you make your health information available to top researchers - under your own terms.

PRIVACY ASSURED

MY DOCTOR OR DISEASE ADVOCACY GROUP RECOMMENDED THIS SERVICE AND PROVIDED ME WITH A REFERRAL #:

Enter referral # here Submit

Privacy Policy Terms of Service Give Feedback

© 2013-2014 Genetic Alliance, Inc. All rights reserved

Everything is ready and because it is patient-centric. It supports both new users as well as individuals who may have started on a different organization's Private Access-enabled site. Everyone benefits!

Public Policy

- Genetic Information Nondiscrimination Act – *led the Coalition that charged the Bill to passage*
- Genetic Testing – *Eyes On the Prize: Truthtelling about Genetic Testing*
- Patenting – *filed an amicus to support innovation and support responsible patenting (Supreme Court)*
- Health Information Technology – *serve on the HIT Standards committee, filed amicus supporting the responsible use of pharmacy data (Supreme Court)*
- Regulation – *Filed citizen's petition to create reasonable oversight of genetic tests*
- Standards – *Work to harmonize ontologies and nomenclature for clinical trials, integrate HL7, LOINC*
- Reimbursement – *Convene payers to determine reasonable evidence levels for diagnostics and therapies in stratified medicine*
- Newborn screening translational network – *collaborate with our Newborn Screening Clearinghouse*

Contact Information

For more information:

Sharon Terry
President and CEO, Genetic Alliance, Inc.
(202) 966-5557, Ext. 201
sterry@geneticalliance.org

General Information: *http://www.geneticalliance.org*