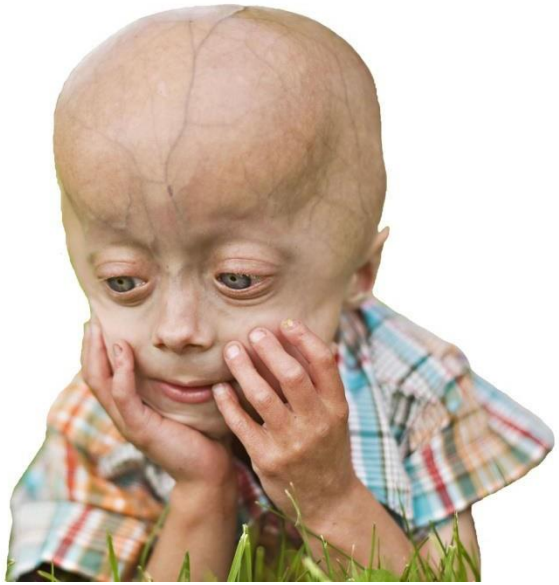
PRF By The Numbers

Progeria Research Foundation

FOR THE CHILDREN ♥ FOR THE CURE



Produced by Leslie B. Gordon, MD, PhD; Medical Director

Table of Contents

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF By The Numbers: A Data Sharing Tool

- PRF By The Numbers is a **data sharing tool** originating from The Progeria Research Foundation's programs and services.

- We translate information collected within our programs and services, and develop charts and graphs which track our progress from year to year.

- This allows you to assess where we've been, and the improvements we've made for children with Progeria.

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Why Sharing Data Is Essential

- According to the National Institutes of Health:

  "data sharing is essential for expedited translation of research results into knowledge, products, and procedures to improve human health."

  http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html

- In other words, everyone benefits by knowing and learning as much as possible about Progeria - the scientific and medical communities, the public, and the children.

NIH National Institutes of Health
Turning Discovery Into Health

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF By The Numbers…Here's How It Works

➢We take raw data collected through our programs and services, remove any personal information to protect the participant, and present it to you in a format that is engaging and informative.

➢ PRF programs and services include:

- The PRF International Registry
- The PRF Diagnostics Program
- The PRF Cell & Tissue Bank
- The PRF Medical & Research Database
- PRF Research Grants
- Scientific Workshops
- Clinical Trial Funding and Participation

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

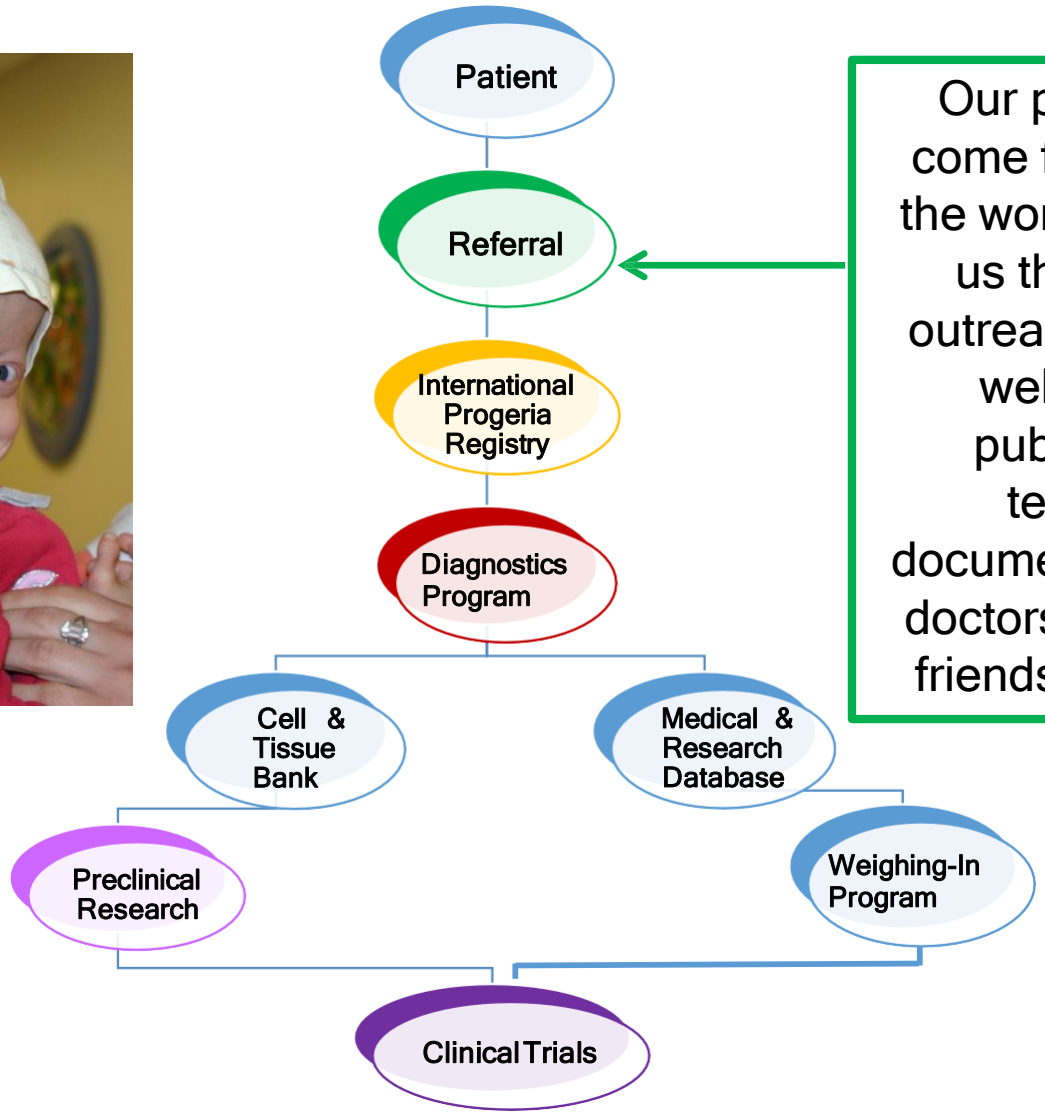
Our Target Audience

- PRF By The Numbers is intended for a broad array of users
  - Families and children with Progeria
  - The general public and nonscientists of all ages
  - Scientists
  - Physicians
  - The media
- This means that different types of slides will be of interest depending on who is looking at the information. We have designed this slide set so that you can pull out what is most important to you.
- We love suggestions - if you don't see some facts and figures here that you think would be informative, please let us know at

info@progeriaresearch.org

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

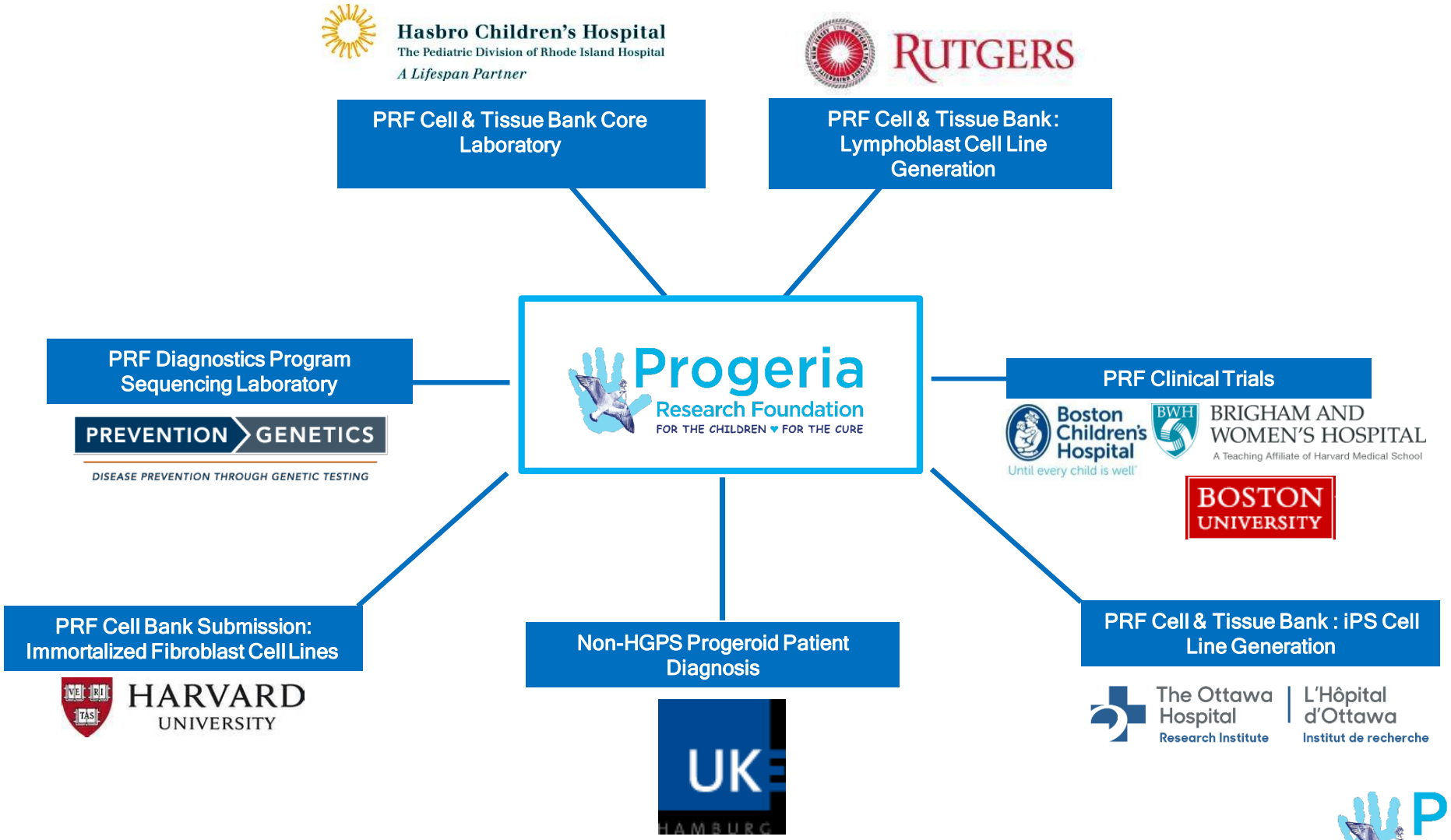
PRF Programs: It All Starts With The Children



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

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Program Collaborations For Success



Our Program Collaborators

Our collaborating institutions are crucial to our ability to help children with Progeria. We are extremely grateful for these ongoing partnerships:

- Hasbro Children's Hospital
  - Location of The PRF Cell & Tissue Bank
  - Program IRB approval

- PreventionGenetics
  - CLIA*-approved genetic sequence testing

- Ottawa Hospital Research Institute
  - Induced Pluripotent Stem Cell (iPSC)
  - CLIA*-approved generation and distribution

Our Clinical Trial Collaborators

Our collaborating institutions are crucial to our ability to help children with Progeria

- Harvard University – Associated Hospitals:
  - Boston Children's Hospital
  - Brigham and Women's Hospital
  - Dana Farber Cancer Institute

- NIH – funded Clinical and Translational Study Unit at Boston Children's Hospital

Number of Living PRF-Identified Cases

December 31, 2023

Total Number of Children with HGPS* and PL** Worldwide: 196

HGPS* worldwide: 144

HGPS* in the United States: 16

Progeroid Laminopathies** worldwide: 52

Progeroid Laminopathies** in the United States: 12

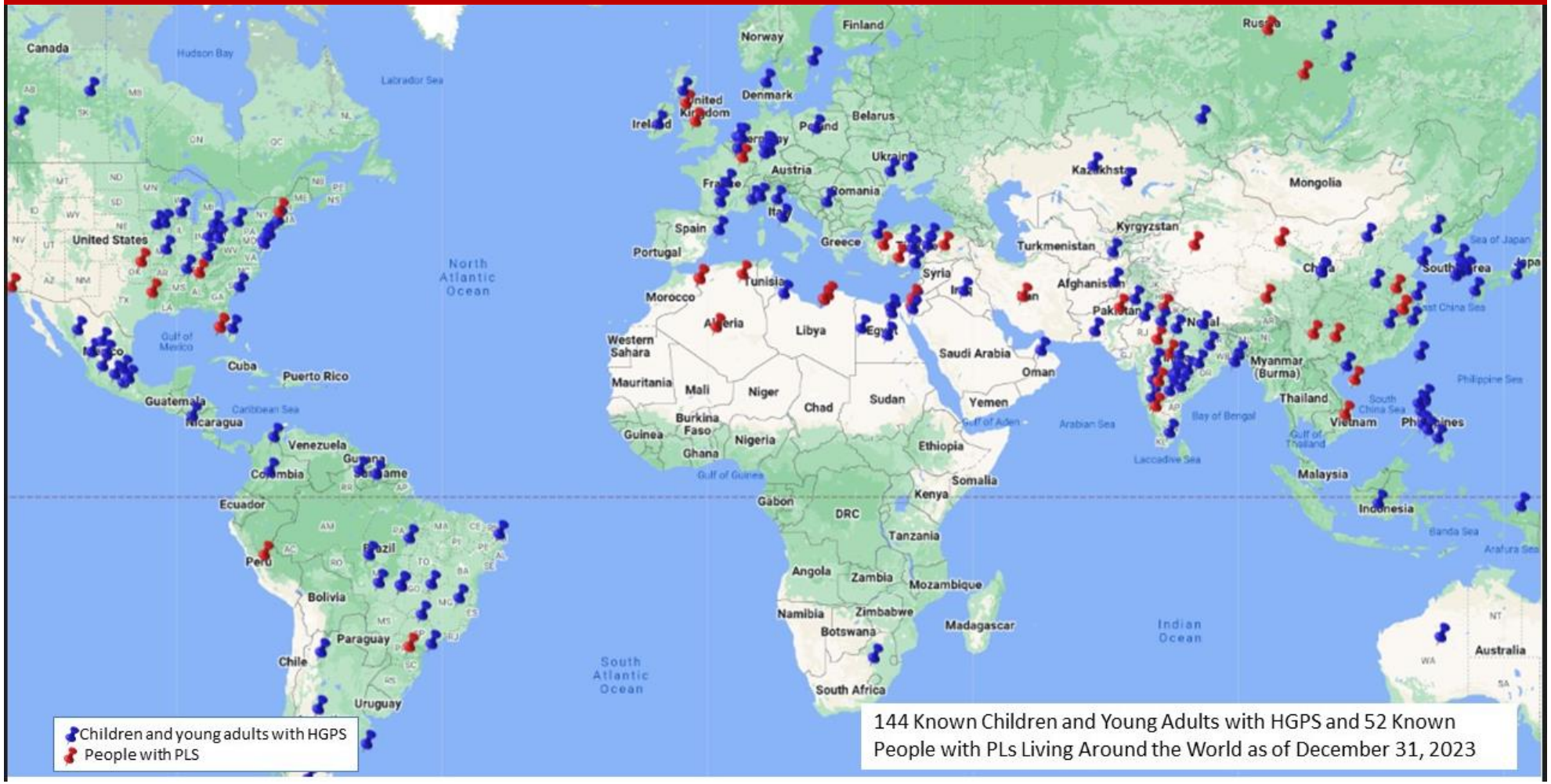
*Children in the HGPS category have a progerin-producing mutation in the LMNA gene

**Those in the Progeroid Laminopathy category have a mutation in the lamin pathway but don't produce progerin
**Cases of PL do not include those identified solely from published scientific journal articles

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF-Identified People Living with HGPS & PL Reside In 50 Countries

Afghanistan
Algeria
Argentina
Australia
Bangladesh
Belgium
Brazil
Canada
China
Colombia
Denmark
Egypt
Ethiopia
France
Germany
Guyana
Honduras
India
Indonesia
Iran
Iraq
Ireland
Israel
Italy



Japan
Kazakhstan
Libya
Luxembourg
Mexico
Nepal
Netherlands
Oman
Pakistan
Palestine-Gaza
Papua New Guinea
Peru
Philippines
Poland
Russia
Serbia
South Africa
South Korea
Spain
Suriname
Sweden
Tajikistan
Turkey
Ukraine
United Kingdom
USA

Note that previous versions of PRF By the Numbers have also reported on cases of PL solely from the literature. These cases are no longer included in this report

...and Speak 34 Languages

Afrikaans	Dutch	Indonesian	Marathi	Russian	Turkish
Arabic	English	Italian	Nepali	Serbain	Ukrainian
Bengali	French	Japanese	Pashto	Spanish	Urdu
Cebuano	German	Kannada	Polish	Tagalog	Yiddish
Chinese	Hebrew	Korean	Portuguese	Tamil	
Danish	Hindi	Malayalam	Punjabi	Tok Pisin	

прогерии исследовательский фонд

خيثلا ثاحبأ ةسسؤم

조로증 연구 재단

早衰症研究基金會

Progeria Araştırma Vakfı

Progeria रिसिच फाउंडेशन

早老症研究財団

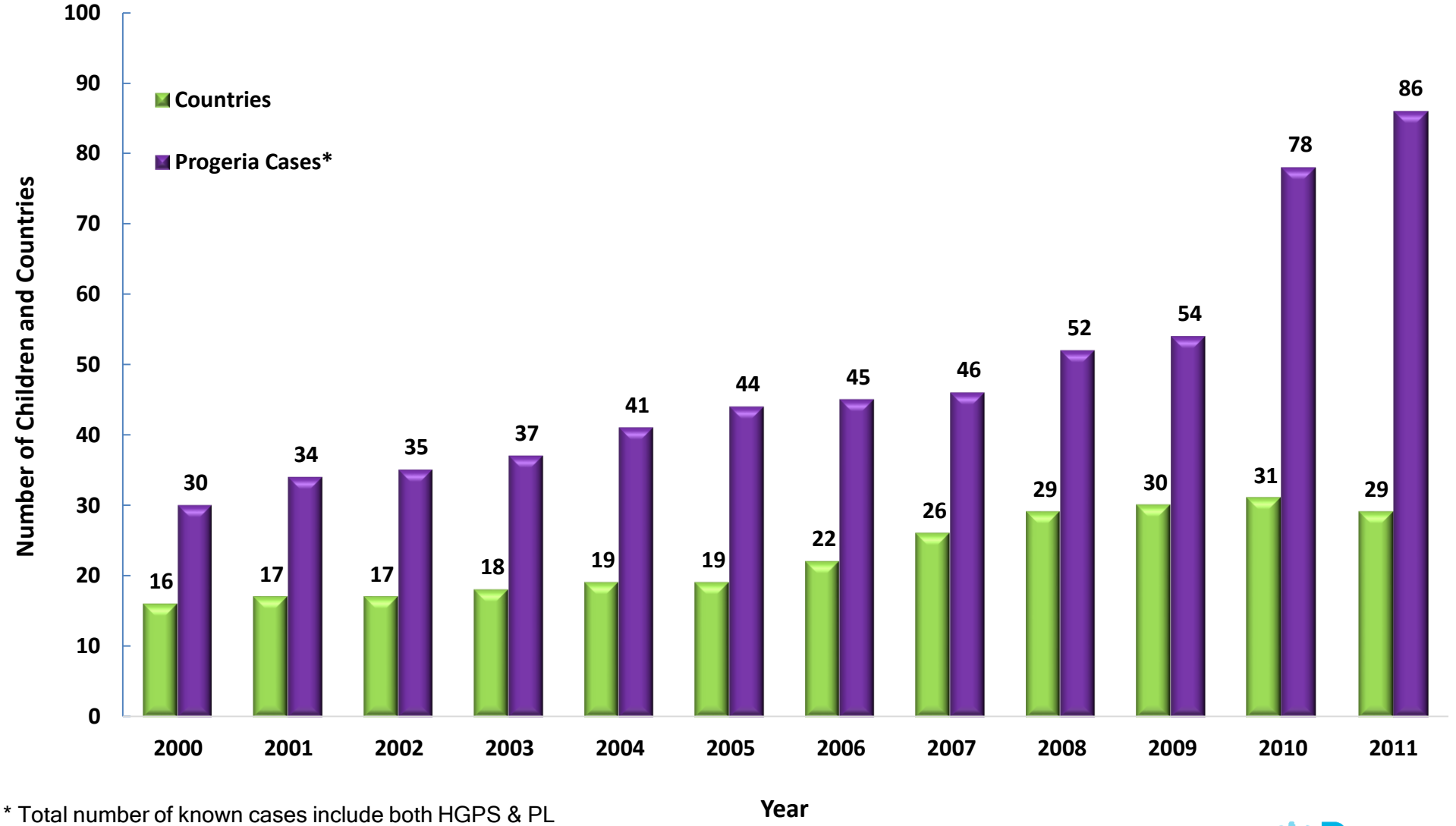
బాలుడ బాలికవయస్సముదరుకండానేవ్యద్ాప్యయూప్ంయోకి
వచ్చుటరసీర్చఫు ండేషన్

December 31, 2023

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Every Year Our Numbers Grow

Living Children and Adults PRF has identified with Progeria and the countries they reside in from 2000 - 2011

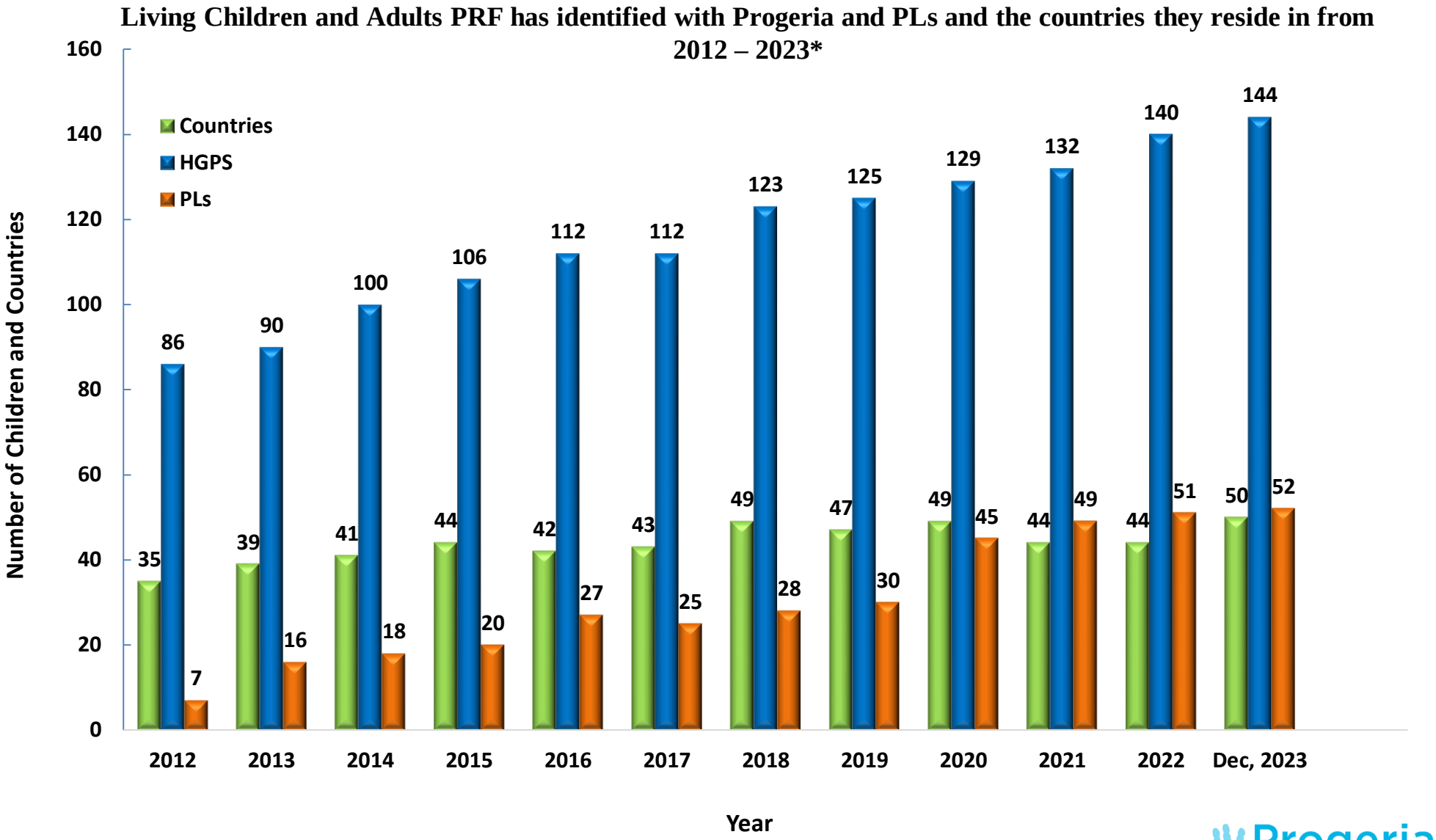


* Total number of known cases include both HGPS & PL
* When a child passes away, numbers are decreased

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

December 31, 2023

Every Year Our Numbers Grow



- Cases of PL do not include those identified solely from published scientific journal articles
- When a child passes away, numbers are decreased

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Tracking Children with Progeria Through Prevalence

- How does PRF estimate how many children we are searching for, and in what countries? We use ***population prevalence***.

- Prevalence is the proportion of children with Progeria per total population.

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

How Prevalence Is Estimated

- At PRF, we use a formula based on the number of children we've identified in the US. We then expand that out to the world population.

- We do this because we have the most complete reporting for the US and since Progeria has no gender, ethnic, or other biases, we assume that the prevalence in the US is the same prevalence in other countries.

- PRF calculates prevalence for the US based on *Worldometer* population estimates.

USA Prevalence of Progeria

December 31, 2023 population statistics:

- The US population is:

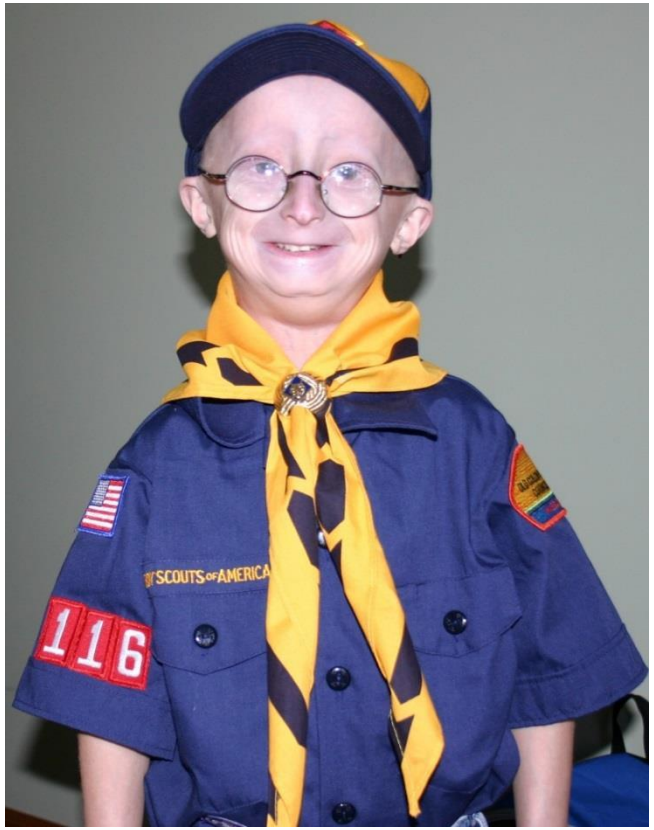
  340,850,921 people

- Number of PRF-identified children with HGPS in the US (3 year average):

  18

- Average prevalence of HGPS in the US:
  18 in 341 million is about

  1 in 19 million people



*estimates routinely fall between 1 in 18 - 1 in 20 million people.

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Prevalence and World Population of Progeria

Given the world population on December 31, 2023

There are between **350** and **450** children living with Progeria worldwide

PRF strives to find every child with Progeria because

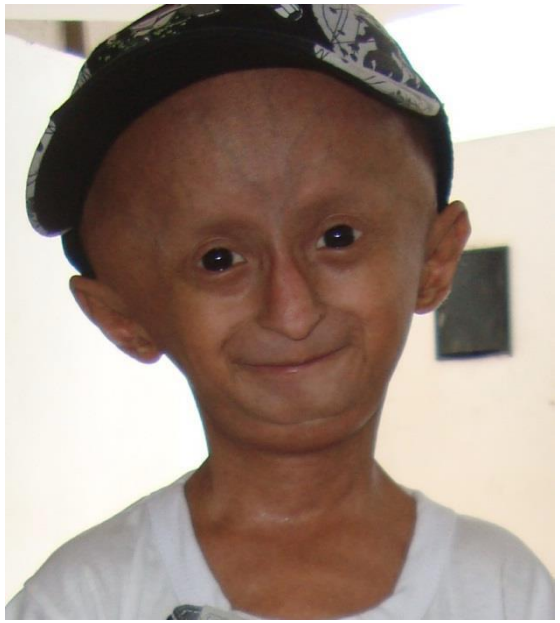
in order to help every child, we must find every child

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Using Prevalence To Find Children In A Certain Country

We can now use the total population estimates for any given country, in order to understand whether we have found most or all children in a particular country.

- For example, as of December 2023:



- Brazil's population was estimated as

216,993,327 people

- Using Prevalence, the number of children living with Progeria in Brazil is 216,993,327/19,000,000 = **11**

- PRF has identified 9 of these 11 children, and is searching for the 2 others

* Data based on the latest *Worldometers* estimates

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

International Progeria Registry*

Program Goals:

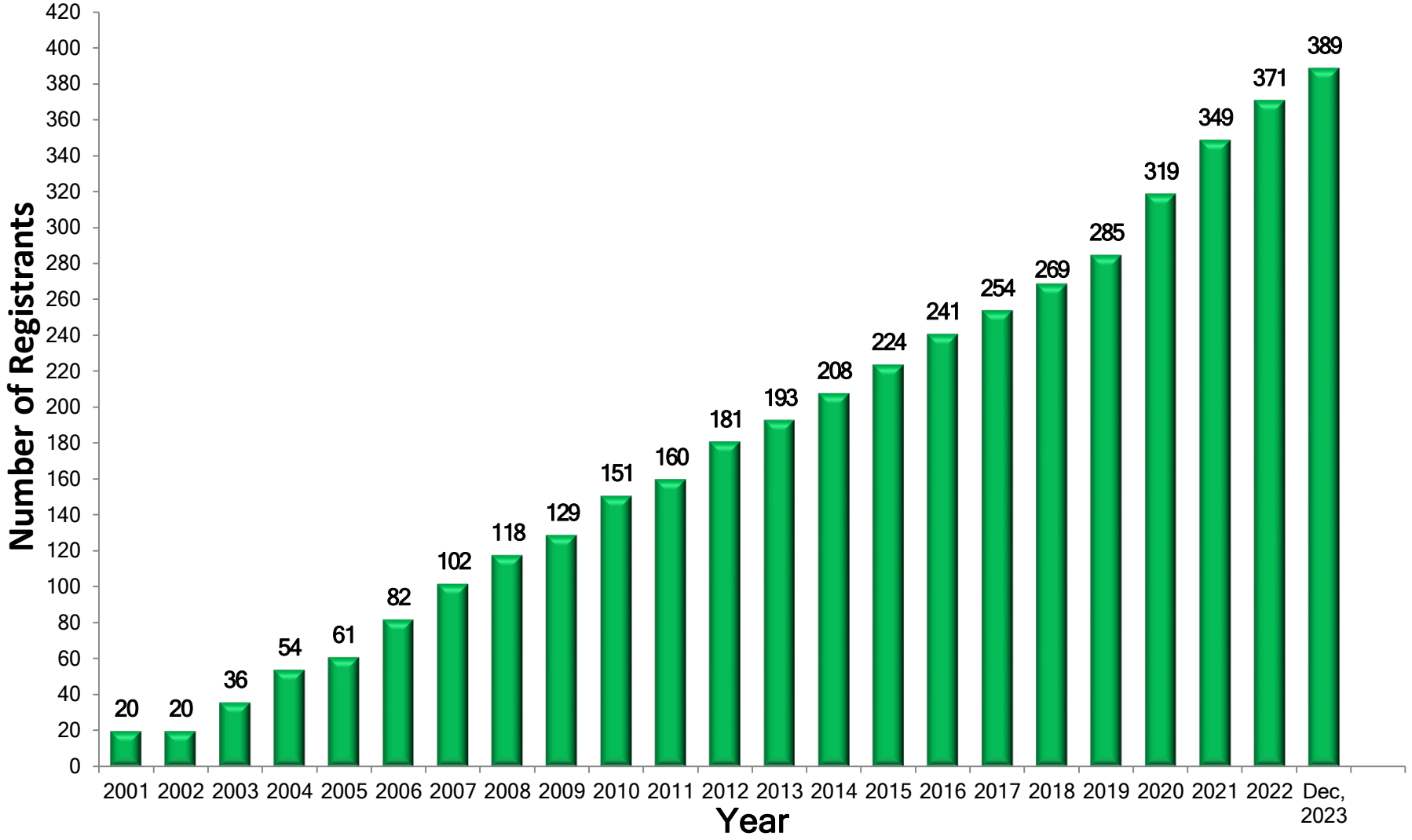
- Patient identification
- Outreach to patient families and their physicians
- A springboard for program enrollment

Registry forms available at
https://www.progeriaresearch.org/international-registry-2/

*PRF International Registry includes those with genetically confirmed or clinically suspected Progeria, as well as those with ZMPSTE24 and other possible progeroid syndromes

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

389 Children and Adults Have Been Registered With PRF



December 31, 2023

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

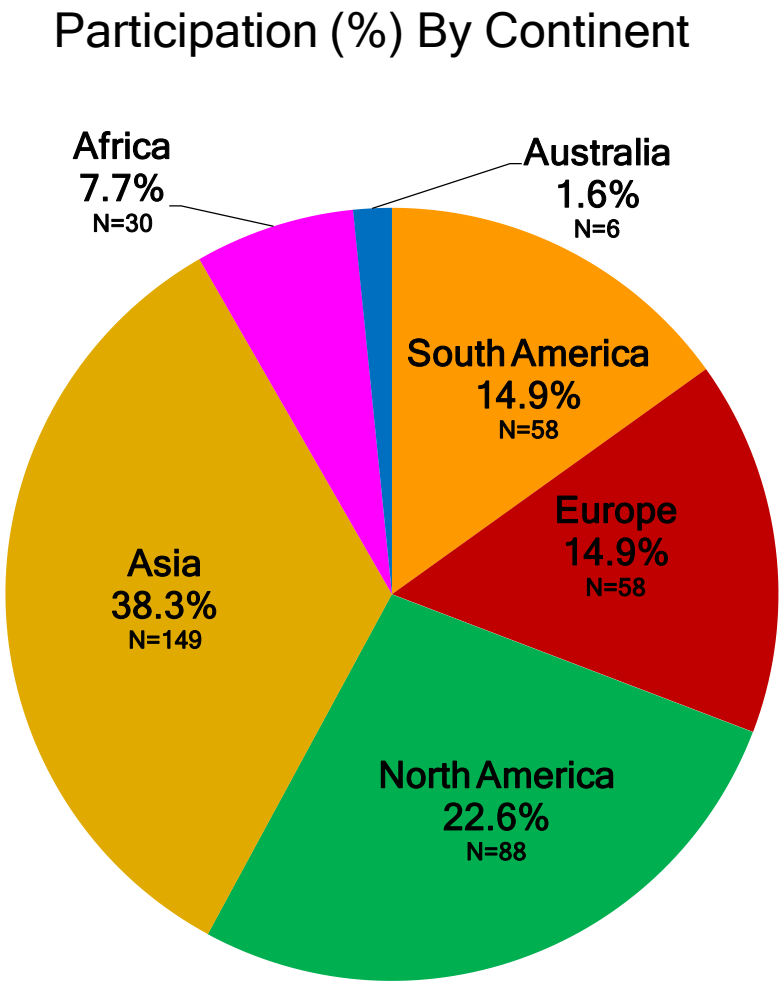
From 72 Countries and 1 Territory

Algeria
Argentina
Australia
Bangladesh
Belgium, Bolivia
Brazil, Bulgaria
Canada, Chile
China, Colombia
Czech Republic
Denmark
Dominican Republic
Ecuador, Egypt
England, Ethiopia,
Finland
France, Germany
Guatemala, Guyana
Honduras
Hong Kong
India, Indonesia
Iran, Iraq
Ireland, Israel
Italy, Japan,
Kazahkstan,
Kyrgyzstan

Libya, Luxembourg
Malaysia, Mexico
Morocco, Nepal
Netherlands
Oman, Pakistan
Palestine
Papua New Guinea
Panama
Peru, Philippines
Poland, Portugal
Puerto Rico
Romania, Russia
Saudi Arabia
Serbia, South Africa
South Korea
Spain, Sri Lanka
Suriname, Sweden
Switzerland,
Tanzania
Thailand, Togo
Turkey, Ukraine
USA, Uzbekistan,
Venezuela
Vietnam

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

…And All Continents

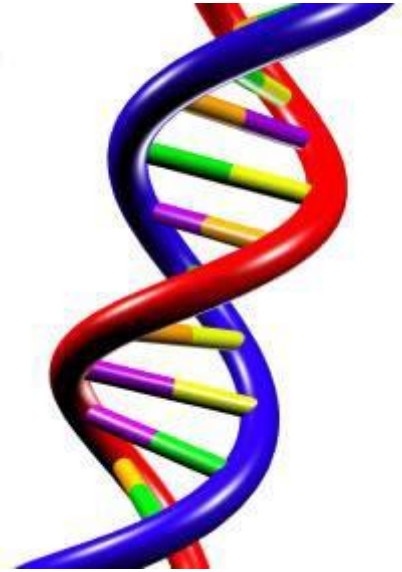


Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF Diagnostics Program

Program Goal:

- Genetic Sequence Testing for Progeria-causing mutations



Pre-requisites for Testing:

- Registration with PRF International Registry
- One or more of the following
  - Family history – proband, prenatal
  - Phenotypic presentation – proband, postnatal
  - Relative of positive proband

Testing information available at:

https://www.progeriaresearch.org/the-prf-diagnostic-testing-program/

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Diagnostics Testing Summary

December 31, 2023

Total Number of Proband Tests Performed: 167

Exon 11 (HGPS) Mutations: 117

Other Progeroid Laminopathies (Exons 1 – 12): 13

ZMPSTE24 Mutations : 2

Average Number of Patients Tested Per Year : 8

All tests are performed in a Clinical Laboratory Improvement Amendments (CLIA) certified facility.

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

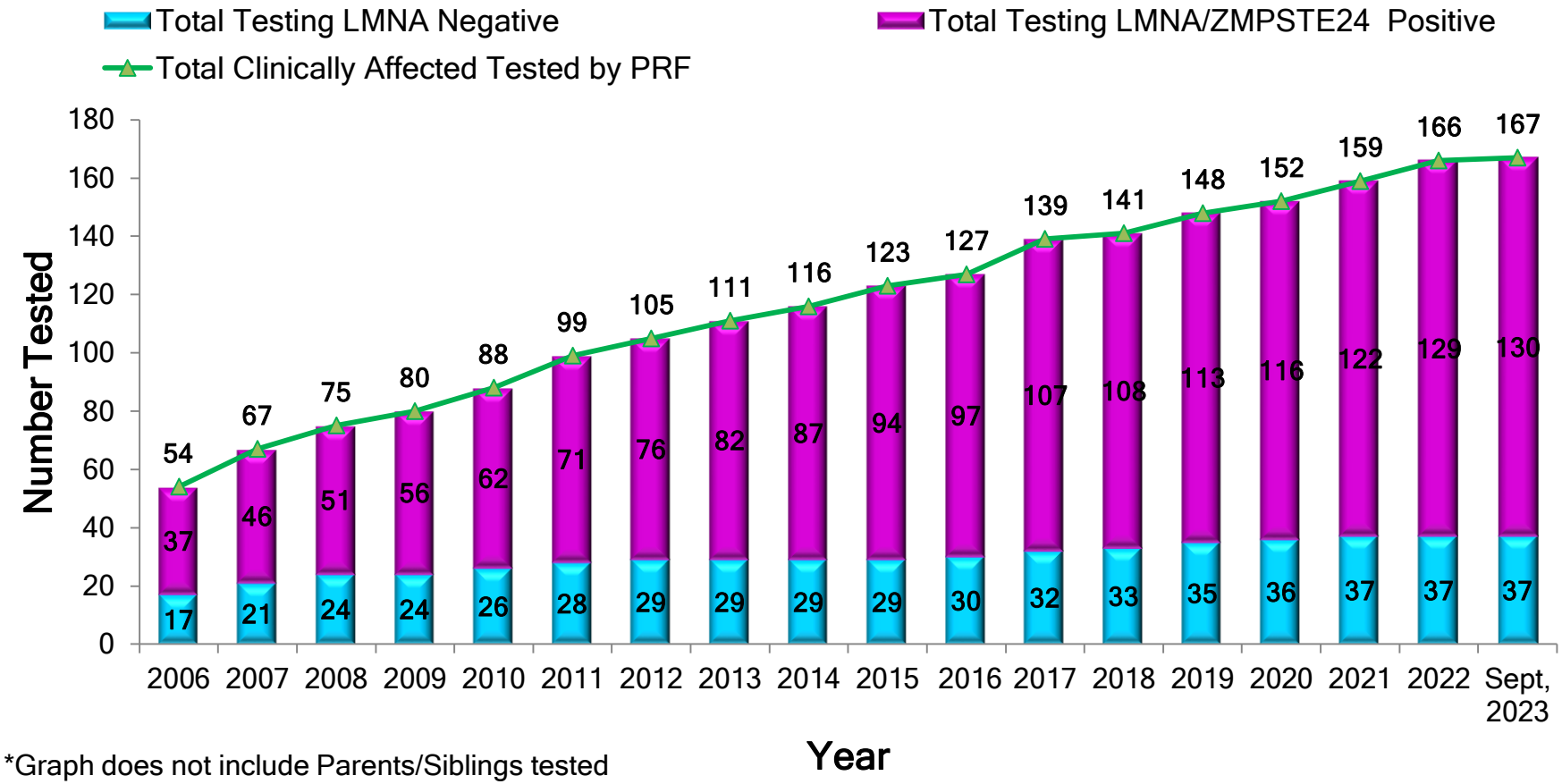
Mutations Identified Through PRF Diagnostics Program

DNA Mutation	Amino Acid Effect	Zygosity	Progerin Producing?	Number Diagnosed
Classic HGPS - LMNA Mutation				
1824 C>T, exon 11	G608G	heterozygous	Yes	103
Non Classic HGPS- LMNA Mutation				
1822 G>A, exon 11	G608S	heterozygous	Yes	4
1821 G>A, exon 11	V607V	heterozygous	Yes	2
1868 C>G, exon 11	T623S	heterozygous	Yes	1
1968+5 G>C, intron 11	None	heterozygous	Yes	2
1968+1 G>C, intron 11	None	heterozygous	Yes	3
1968+2 T>A, intron 11	None	heterozygous	Yes	1
1968+1 G>A, intron 11	None	heterozygous	Yes	1
Progeroid Laminopathy- LMNA Mutation				
1579 C>T, exon 9	R527C	heterozygous	No	1
1579 C>T, exon 9	R527C	homozygous	No	6
1580G>T, exon9	R527L	Homozygous	No	2
1619 T>C, exon 10	M540T	homozygous	No	3
331 G>A, exon 1	E111K	heterozygous	No	1
Progeroid Laminopathy- ZMPSTE2424 Mutation				
1274T>C, exon 10	L425P	homozygous	No	2

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Longitudinal Testing Data for PRF Diagnostics Program

Number of Affected Children/Adults Tested and the Number Testing Positive for *LMNA* Gene Mutation*



*Graph does not include Parents/Siblings tested

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF Cell & Tissue Bank

Program Goals:

- Provide a resource for researchers worldwide
- Ensure the sufficient availability of genetic and biological materials essential for research aimed at understanding the pathophysiology of disease and the links between Progeria, aging and heart disease
- Obtain long-term clinical data

Resource information available at: https://www.progeriaresearch.org/cell-and-tissue-bank/

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF Cell and Tissue Bank Holdings

As of December 31, 2023

Total Number of Participants: 361*

71 Dermal Fibroblast Lines from 47 affected and 24 parents

6 Immortalized Fibroblast Cell Lines from 1 affected and 5 parents

126 Lymphoblast Lines from 71 affected, 47 parents and 8 siblings

9 Induced Pluripotent Stem Cell Lines from 5 affected and 4 parents

* Participants may have donated multiple times

* Additional sample types are available for special projects upon request

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Mutations Available in PRF Cell & Tissue Bank

DNA Mutation	Amino Acid Effect	Zygosity	Progerin Producing?	Cell Type DFN=Dermal Fibroblast LBV= Lymphoblast
Classic HGPS - LMNA Mutation				
c.1824 C>T, exon 11	p.G608G	heterozygous	Yes	DFN, LBV, iPSC
Non Classic HGPS- LMNA Mutation				
c.1822 G>A, exon 11	p.G608S	heterozygous	Yes	DFN, LBV
c.1821 G>A, exon 11	p.V607V	heterozygous	Yes	LBV
c.1824 C>T, exon 11 & SMC3 c.562 A>G	p.G608G & p.K188E	heterozygous	Yes	DFN
c.1868 C>G, exon 11	p.T623S	heterozygous	Yes	LBV
c.1968+5 G>C, intron 11	---------	heterozygous	Yes	DFN
c.1968+5 G>A, intron 11	---------	heterozygous	Yes	DFN
c.1968+1 G>A, intron 11	---------	heterozygous	Yes	DFN, LBV
c.1968+2 T>C, exon 11	---------	heterozygous	Yes	DFN
c.1968+2 T>C, exon 11 & c.1968+2 T>A, exon 11	---------	heterozygous	Yes	DFN
Progeroid Laminopathy- LMNA Mutation				
c.1579 C>T, exon 9	p.R527C	heterozygous	No	LBV
c.1579 C>T, exon 9	p.R527C	homozygous	No	LBV
c.1580 G>T, exon 9	p.R527L	homozygous	No	LBV
c.1619 T>C, exon 10	p.M540T	homozygous	No	DFN
c.1762 T>C, exon 11	p.C588R	heterozygous	No	DFN
c.1930 C>T, exon 11	p.R644C	heterozygous	No	DFN
c.331 G>A, exon 1 & c.1158-44 C>T, intron 6	p.E111K	heterozygous	No	DFN, LBV
c.412 G>A	p.E138K	heterozygous	No	DFN
c.973 G>A, exon 6	p.D325N	heterozygous	No	DFN
Progeroid Laminopathy- ZMPSTE2424 Mutation				
c.1274 T>C, exon 10	p.L425P	homozygous	No	DFN, LBV
c.743 C>T, exon 6 & c.1349 G>A, exon 10	p.P248L & p.W450Stop	heterozygous	No	DFN

PRF Cell & Tissue Bank Distribution

As of December 22, 2023:

237 Research Teams From **29** Countries Have Received

1534 Cell Lines

204 DNA Samples

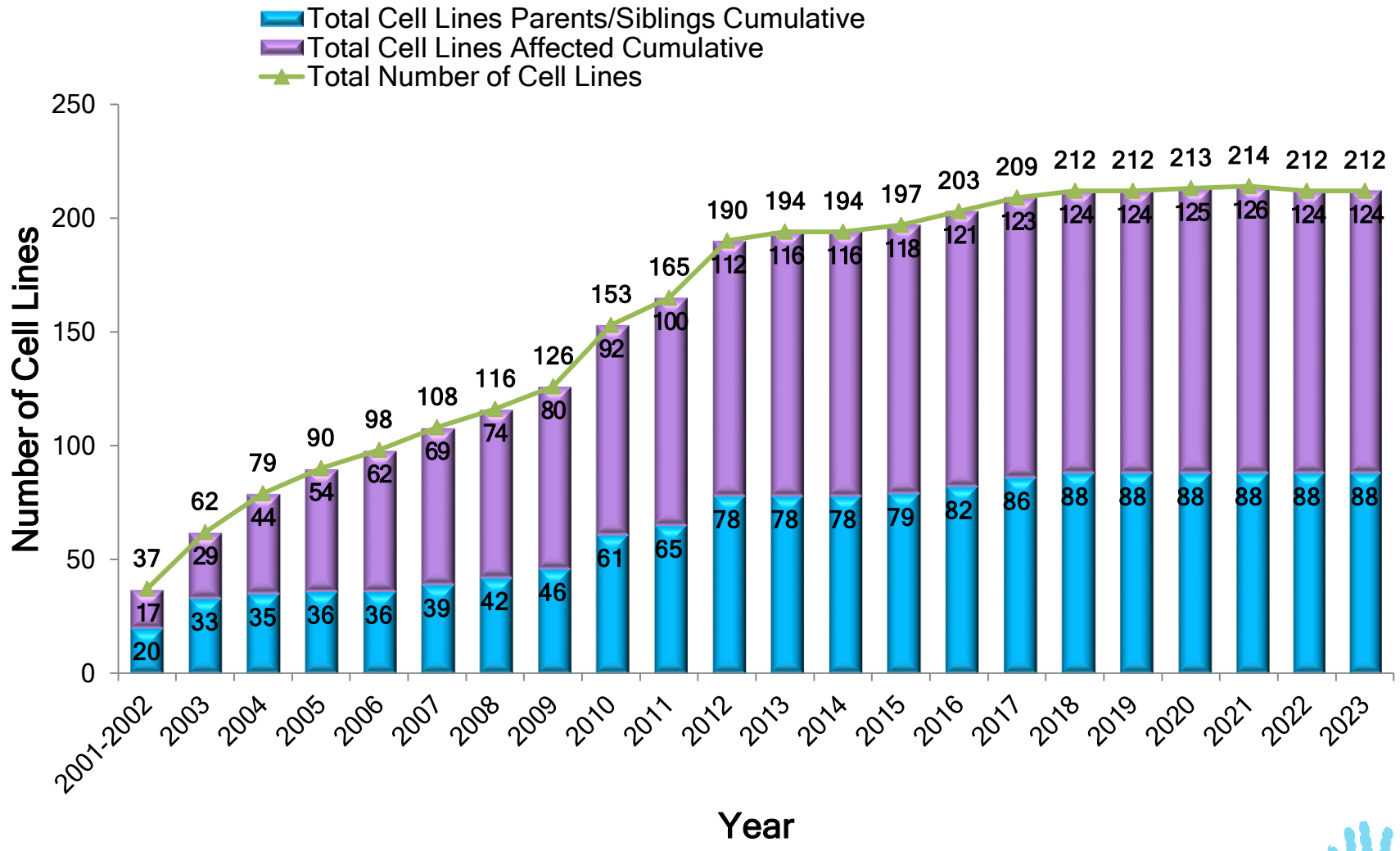
455 Tissue, plasma, serum and other biological samples

32 Lonafarnib Samples

Senescent Progeria Fibroblasts in Culture

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

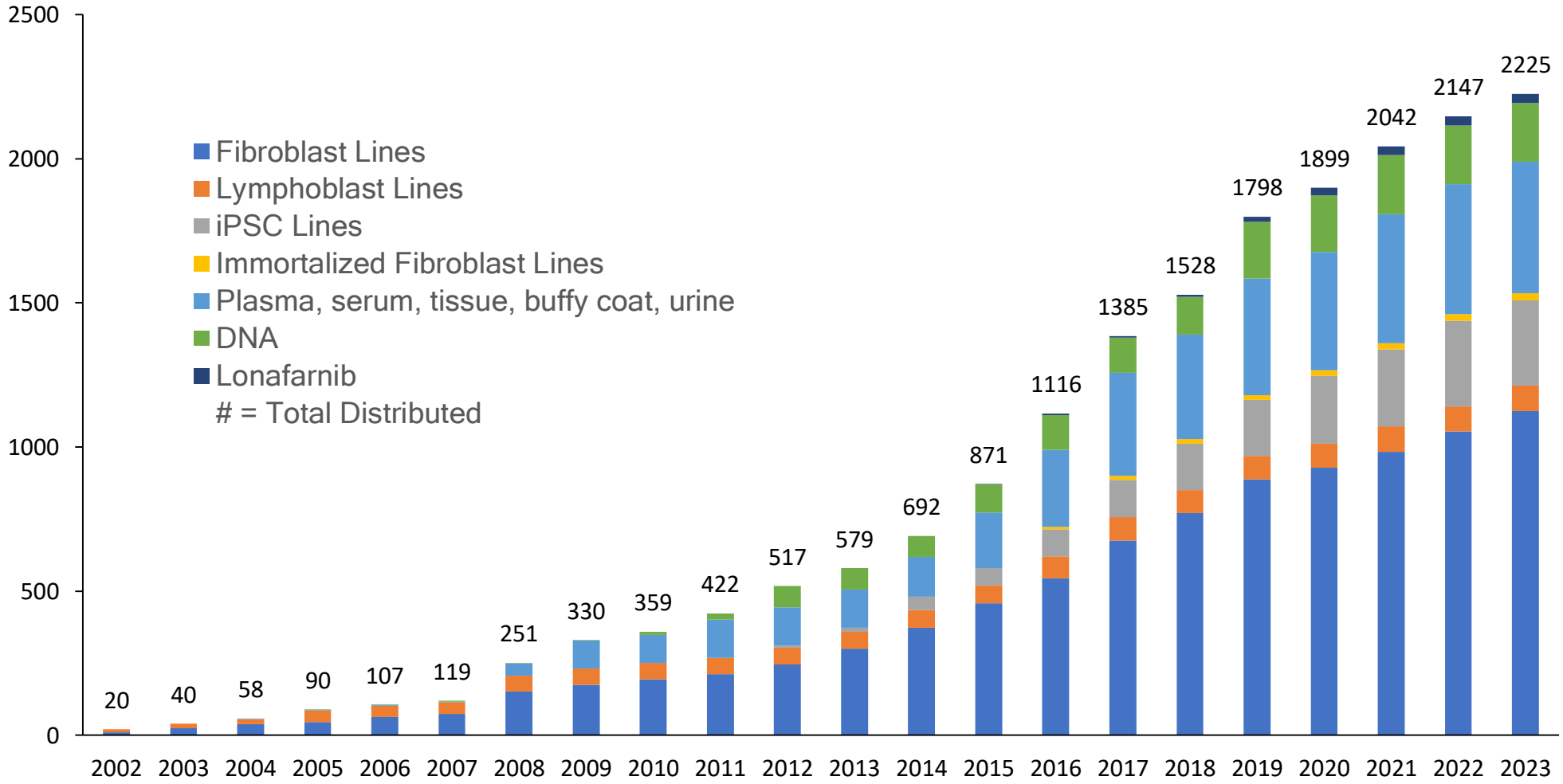
Number Of Cell Lines By Year



Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

December, 31, 2023

Cumulative Number of Biological Samples Distributed

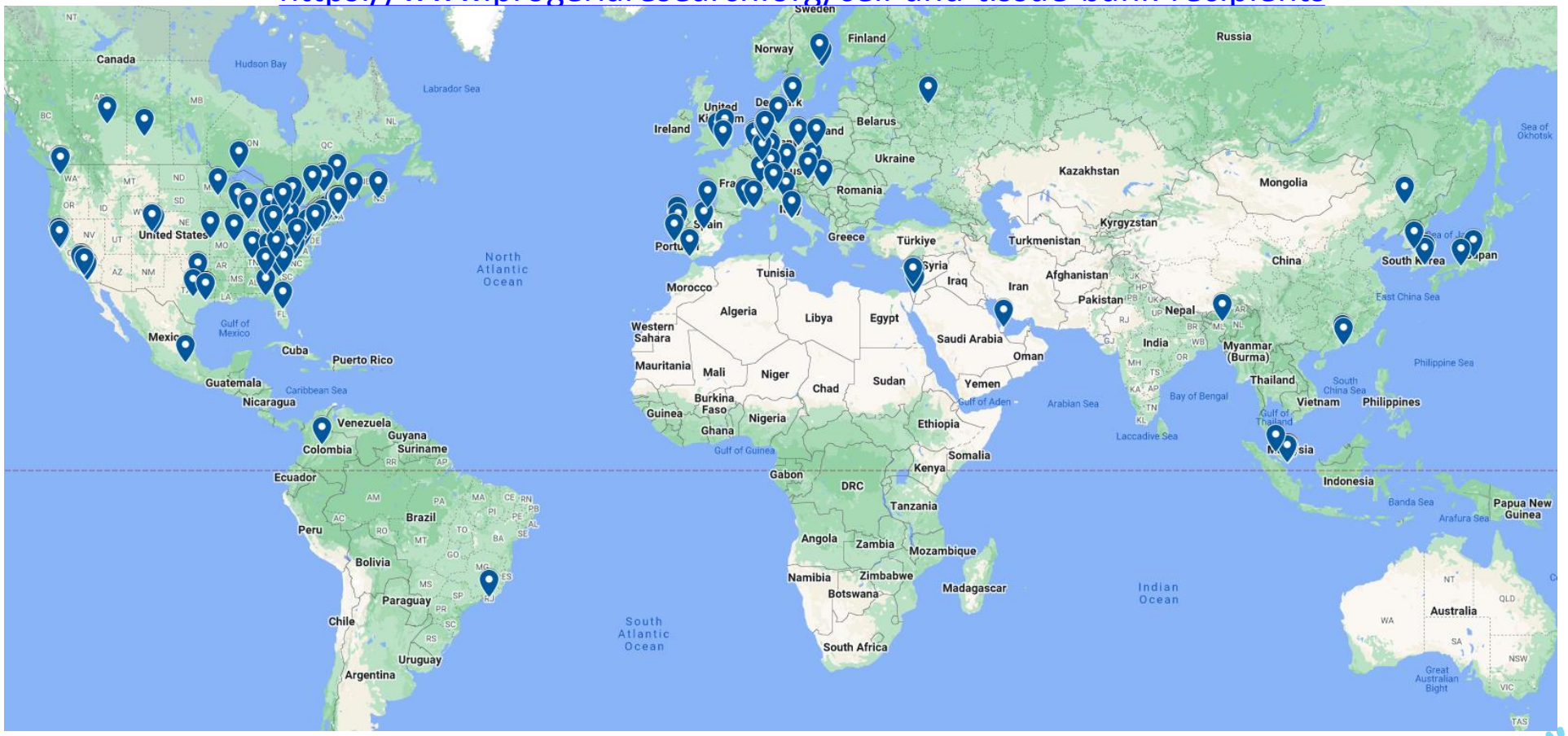


Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

December 31, 2022

Cell and Tissue Bank Recipients

Cells and biological material have been distributed to
237 laboratories in **29** countries
Complete list of researchers available at:
https://www.progeriaresearch.org/cell-and-tissue-bank-recipients



December 31, 2023

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF Medical & Research Database

Program Goals:

- Collect the patient health records for living and deceased children with Progeria
- Obtain long-term clinical data
- Abstract data for longitudinal and cross-sectional analyses
- Better understand the clinical disease process in Progeria and aging related diseases
- Develop treatment strategies and recommendations for health care professionals and families

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

How The PRF Medical & Research Database Works

- Project staff obtain the patient's medical records and film studies from birth throughout the participant's lifespan.
- Medical records include visits to: primary care physicians, specialty physicians, hospital emergency rooms, hospital admissions, dentists, physical therapy, occupational therapy and school health records.
- Retrospective data abstraction protocol allows for specifically targeted or broad spectrum of data.

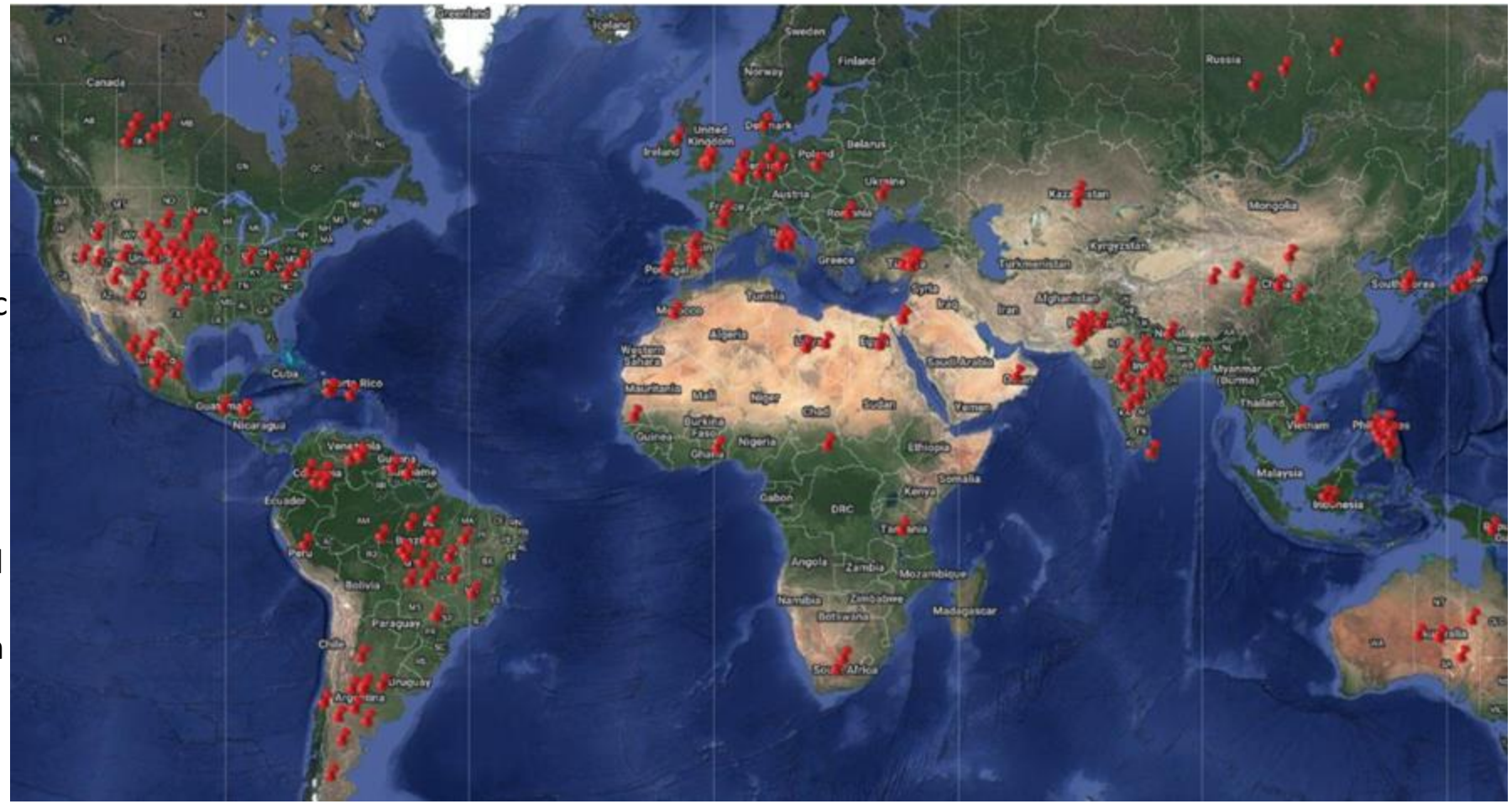
Enrollment information available at: https://www.progeriaresearch.org/medical-database/

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Medical & Research Database Participation

221 Participants are enrolled from **55** countries and **1** US territory

Algeria
Argentina
Australia
Bangladesh
Belgium Brazil
Canada, Chile
China, Columbia
Denmark
Dominica Republic
Egypt, England
France, Germany
Guatemala,
Guyana
Honduras, India
Indonesia, Ireland
Israel, Italy
Japan, Kazakhstan

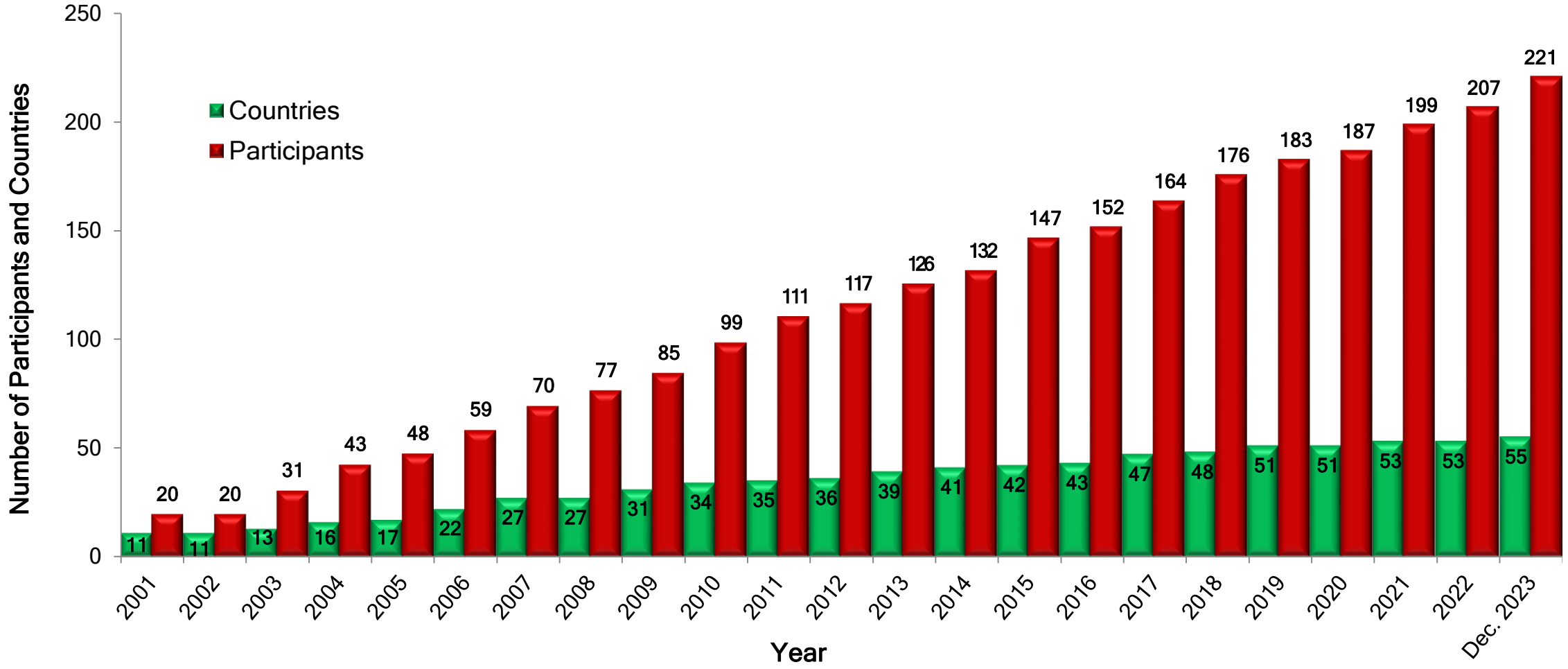


Libya, Mexico
Morocco, Nepal
Netherlands
Oman, Pakistan
Papua New Guinea
Peru, Philippines
Poland, Portugal
Puerto Rico
Romania, Russia
Senegal, Serbia
South Africa
South Korea
Spain, Sri Lanka
Suriname, Sweden
Tanzania, Togo
Turkey, Ukraine
USA, Venezuela
Vietnam

December 31, 2023

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Medical & Research Database Longitudinal Enrollment

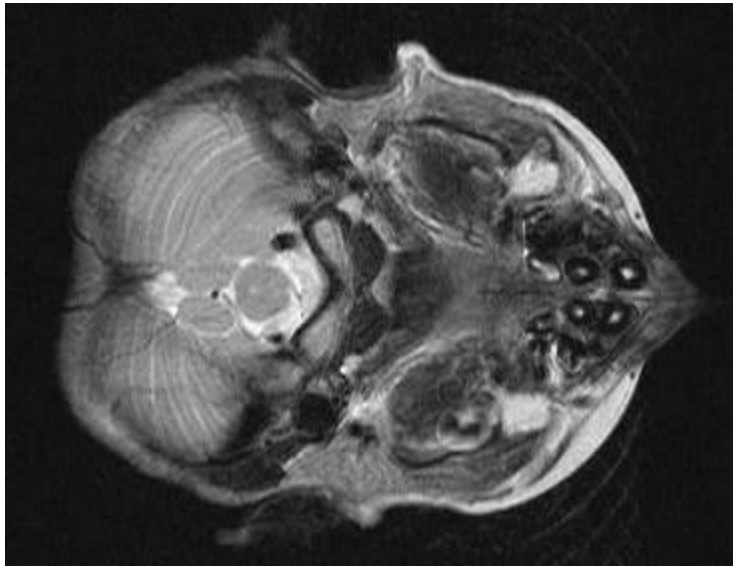


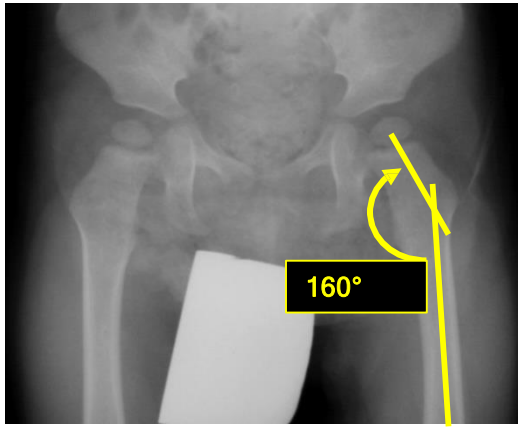
December 31, 2023

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Types Of Data Collected

- Participants with Medical Records Reports: **166**
- Participants with Radiology Studies: **65**





Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF Weighing-In Program

- A sub-program of The PRF Medical & Research Database
- Collects weight-for-age data prospectively:
  - Home scale provided by PRF
  - Parents weigh child weekly or monthly
  - Report weights electronically

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Weighing-In Program Participation

122

Participants are enrolled from 42 countries and 1 US territory

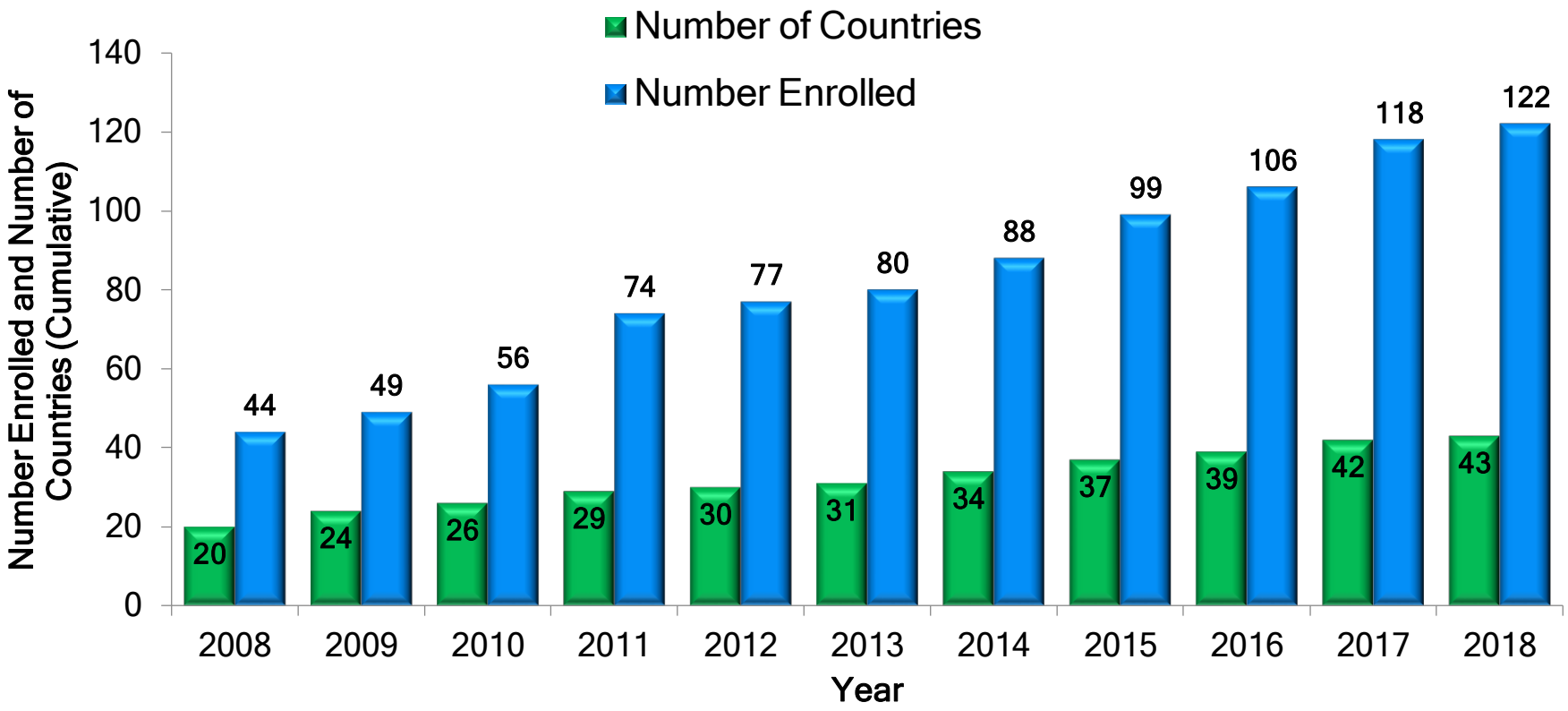
Argentina
Australia
Bangladesh
Belgium
Brazil
Canada
China
Colombia
Denmark
Dominion Republic
England
Germany
Guatemala
Honduras
India
Indonesia
Ireland
Israel
Italy
Japan
Mexico
Morocco

Nepal
Pakistan
Peru
Philippines
Poland
Portugal
Puerto Rico
Romania
Russia
Senegal
South Africa
South Korea
Spain
Sri Lanka
Togo
Tanzania
Turkey
Ukraine
USA
Venezuela
Vietnam

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

December 31, 2023

Participants Enrolled In The PRF Weighing-In Program and Countries of Residence



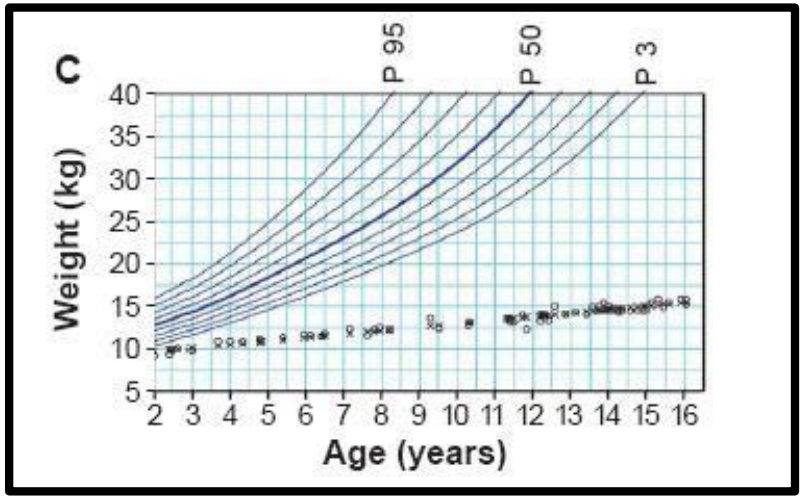
December 31, 2023

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Clinical Trials And The Weighing-In Program

- Data from this program were key in the development of primary outcome measure for the first drug treatment trial for Progeria.

- As of December 1, 2018, 90 children from The PRF Weighing-In Program have entered clinical treatment trials using this data.



Failure to Thrive Starts Towards End of Year One

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

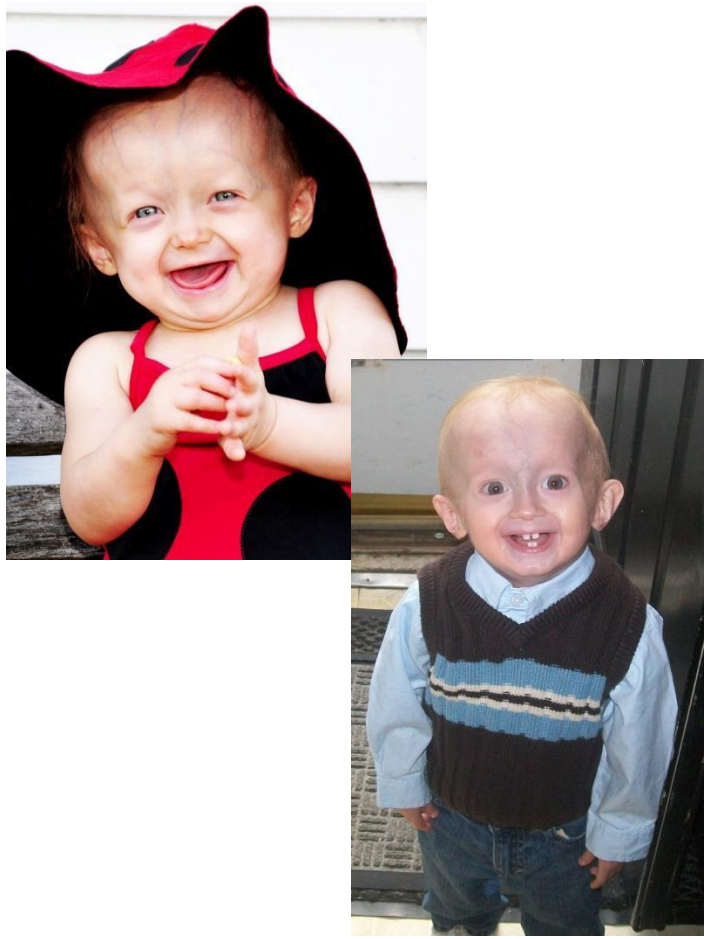
PRF-Funded Clinical Treatment Trials

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Clinical Drug Treatment Trials

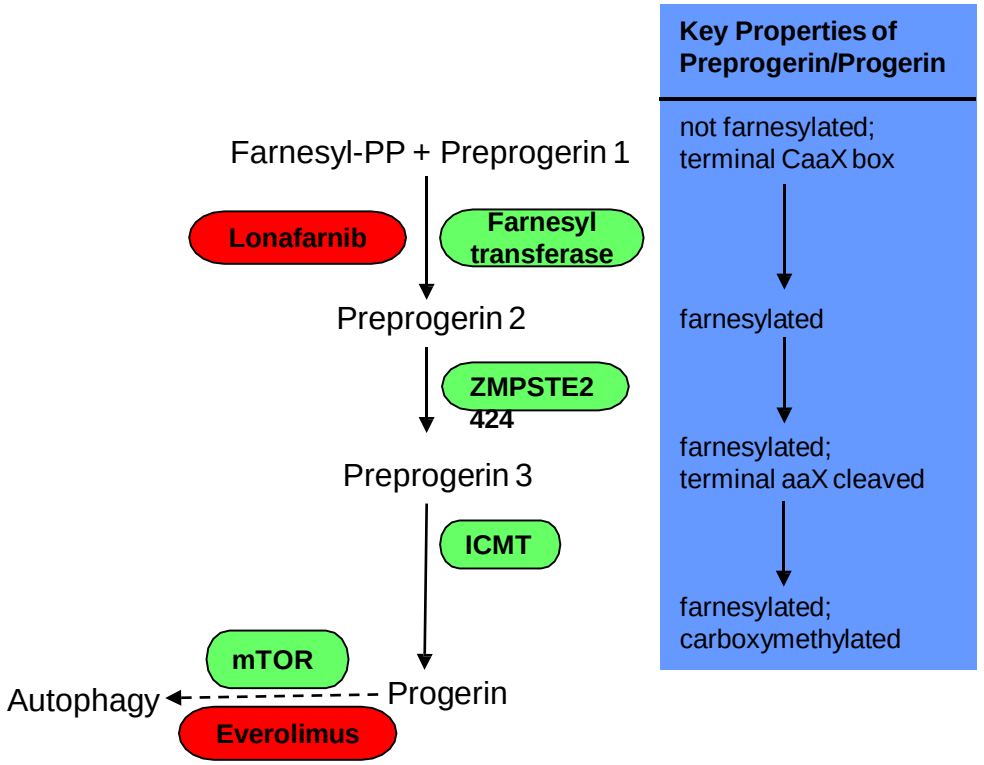
Goals:

- To define the natural history of HGPS in quantifiable terms that will expand our ability to measure treatment outcome
- To assess the safety of new treatments for HGPS
- To measure effects of treatments for children with HGPS on disease status, changes in health, and survival



Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Current Therapeutic Intervention Strategies



Post-translational processing and medications currently under investigation in clinical treatment trials for Progeria. Items in green = enzymes. Items in red = clinical trial medications that inhibit corresponding enzymes. Lonafarnib is a farnesyltransferase inhibitor. Everolimus is a rapamycin analogue that inhibits mTOR and promotes cellular autophagy. FT=farnesyltransferase.

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF Funds Clinical Treatment Trials

Year	Drug(s)	Phase	Location	#	Countries
2007-2010	Lonafarnib	2	Boston	29	16
2009	Lonafarnib Pravastatin Zoledronate	Feasibility	Boston	5	2
2009 - 2013	Lonafarnib Pravastatin Zoledronate	2	Boston	45	24
2014 - 2021	Lonafarnib	2	Boston	71	32
2016 - 2023	Lonafarnib Everolimus	1/2	Boston	60	27
2018 - present	Lonafarnib	2	Boston	62 from 30 countries enrolled as of December 31, 2023	

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Participation in PRF Clinical Trials

Argentina
Australia
Belgium
Brazil
Canada
China
Colombia
Denmark
Dominican Republic
Egypt
England
Germany
Guyana
Honduras
India
Israel
Italy
Japan
Kazakhstan
Libya
Mexico

107 Children have participated in PRF Clinical Trials from **42** countries

Morocco
Pakistan
Peru
Philippines
Poland
Portugal
Romania
Russia
Serbia
South Africa
South Korea
Spain
Sri Lanka
Suriname
Sweden
Tanzania
Togo
Turkey
Ukraine
USA
Venezuela

December 31, 2023

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

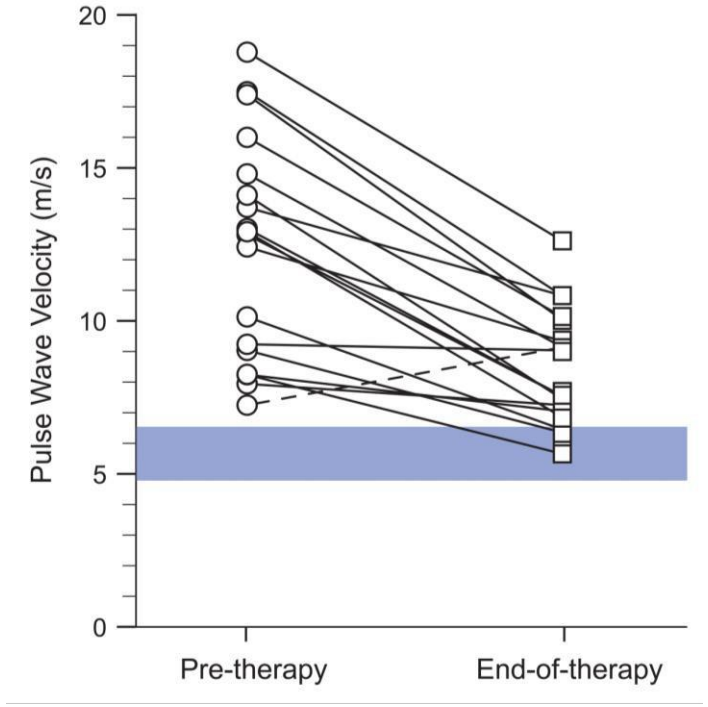
Clinical Treatment Trial Efficacy Results

Lonafarnib, a type of farnesyltransferase inhibitor (FTI) is our first treatment for Progeria.

➢Results showed improvement in:

- Rate of weight gain
- Increased vascular distensibility
- Improved bone structure
- Better neurosensory hearing
- Increased Lifespan

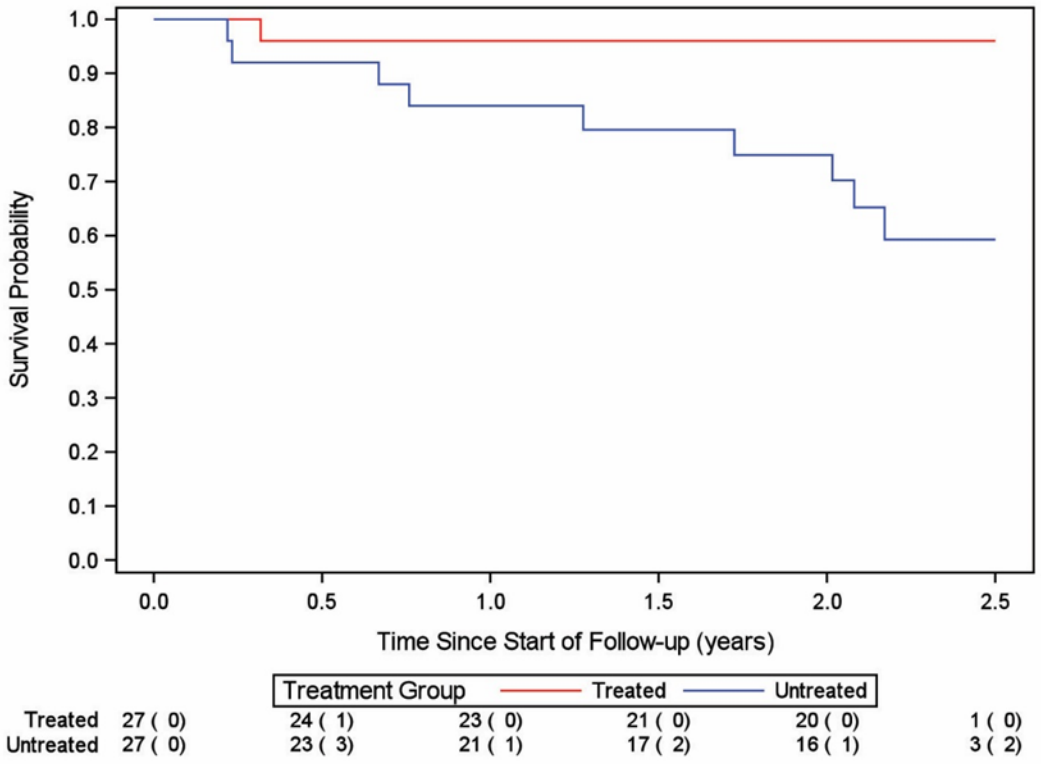
Gordon et al, PNAS, 2011



Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Positive Effects of Lonafarnib (Zokinvy) on Progeria: Results of PRF's Clinical Treatment Trials

- Average increased lifespan of 4.3 years
- Increased vascular distensibility
- Improved bone structure
- Better neurosensory hearing
- Modest increase in rate of weight gain



Gordon et al., PNAS, 2011 and
Gordon et al., JAMA, 2018
Gordon et al., Circulation 2023

JAMA | Preliminary Communication

Association of Lonafarnib Treatment vs No Treatment With Mortality Rate in Patients With Hutchinson-Gilford Progeria Syndrome

Leslie B. Gordon, MD, PhD; Heather Shappell, PhD; Joe Massaro, PhD; Ralph B. D'Agostino Sr, PhD; Joan Brazier, MS; Susan E. Campbell, MA; Monica E. Kleinman, MD; Mark W. Kieran, MD, PhD

3 Ways to Access Lonafarnib (Zokinvy)

Zokinvy (lonafarnib) is an FDA approved drug in the US. It is the current standard of care for those with Progeria. It is available through

1. Prescription in the US and in select non-US countries
2. PRF's clinical treatment trials
3. The manufacturer's (Eiger) Managed Access Program in select non-US countries

We are far from finished!
We must forge ahead with increased intensity and collaborative efforts to find additional treatments, and the cure!

Please contact PRF at info@progeriaresearch.org for more information on how to access Zokinvy (lonafarnib) for your child or patient with Progeria

December 31, 2023

Treatment Trial Collaborations For Success

- **The children are seen by physicians from:**
  - Boston Children's Hospital
  - Dana-Farber Cancer Institute
  - Brigham and Women's Hospital
- **Data were also generated by scientists from:**
  - Alpert Medical School at Brown University
  - Brown University School of Public Health
  - University of California Los Angeles
  - National Human Genome Research Institute
  - Schering-Plough Research Institute
- **Lonafarnib generously provided by Eiger**
- **Everolimus generously provided by Novartis**

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Clinical Trial Publications

Drug Effect:

Plasma Progerin in Patients With Hutchinson-Gilford Progeria Syndrome: Immunoassay Development and Clinical Evaluation. Gordon et al., *Circulation*, 2023;147(23):1734-1744

FDA approval summary for lonafarnib (Zokinvy) for the treatment of Hutchinson-Gilford progeria syndrome and processing-deficient progeroid laminopathies. Suzuki et al., *Genetics in medicine*, 2023;25(2):100335

Association of Lonafarnib Treatment vs No Treatment With Mortality Rate in Patients With Hutchinson-Gilford Progeria Syndrome. Gordon et al., *JAMA*, 2018, 319(16):1687-1695.

Survey of Plasma Proteins in Children with Progeria Pre-therapy and On-Therapy with Lonafarnib. Gordon et al., *Pediatric Research*, 2018;83(5):982-992

Clinical Trial of the Protein Farnesylation Inhibitors Lonafarnib, Pravastatin, and Zoledronic Acid in Children With Hutchinson-Gilford Progeria Syndrome. Gordon et al., *Circulation*, 2016 Jul 12;134(2):114-25.

Seeking a Cure for One of the Rarest Diseases: Progeria. Collins, *Circulation,* 2016 Jul 12;134(2):126-9.

Impact of Farnesylation Inhibitors on Survival in Hutchinson-Gilford Progeria Syndrome. Gordon et al., *Circulation*, 2014 Jul 1;130(1):27-34.

Moving from Gene Discovery to Clinical Trials in Hutchinson-Gilford Progeria Syndrome. King et al., *Neurology*, 2013 Jul 30;81(5):408-9.

Neurologic Features of Hutchinson-Gilford Progeria Syndrome after Lonafarnib Treatment. Ullrich et al., *Neurology*, 2013, 81:427-430.

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.

General:

Clonal hematopoiesis is not prevalent in Hutchinson-Gilford progeria syndrome. Díez-Díez, et al., *GeroScience*. 2023;45(2):1231-1236

Pubertal Progression in Adolescent Females with Progeria. Greer et al., *Journal of Pediatric and Adolescent Gynecology*, 2018;31(3):238-241

Phenotype and Course of Hutchinson-Gilford Progeria Syndrome. Meredith et al., *New England Journal of Medicine*, 2008, 358(6): 592- 604.

Dermatology:

Initial Cutaneous Manifestations of Hutchinson-Gilford Progeria Syndrome. Rork et al., *Pediatric Dermatology*, 2014,1-7.

Clinical Trial Publications Continued

Dental:

Microbiome at Sites of Gingival Recession in Children with Hutchinson-Gilford Progeria Syndrome. Bassir et al., *Journal of Periodontology*. 2018, 89(6): 635-644.

Hutchinson-Gilford Progeria Syndrome: Oral and Craniofacial Phenotypes. Domingo et al., *Oral Diseases*, 2009, 15(3): 187-195.

Cerebrovascular:

Imaging Characteristics of Cerebrovascular Arteriopathy and Stroke in Hutchinson-Gilford Progeria Syndrome. Silvera et al., *American Journal of Neuroradiology*, 2013 May;34(5):1091-7.

Cardiology:

Progression of Cardiac Abnormalities in Hutchinson-Gilford Progeria Syndrome: A Prospective Longitudinal Study. Olsen FJ, et al. *Circulation*. 2023;147(23):1782-1784.

Cardiac Abnormalities in Patients With Hutchinson-Gilford Progeria Syndrome. Prakask, et al., *JAMA Cardiology*, 2018, Apr 17;115(16):4206-4211.

Mechanisms of Premature Vascular Aging in Children with Hutchinson-Gilford Progeria Syndrome. Gerhard-Herman M, et al., *Hypertension*. 2012; 59(1):92-97.

Skeletal:

Baseline Range of Motion, Strength, Motor Function, and Participation in Youth with Hutchinson-Gilford Progeria Syndrome. Malloy et al., *Phys Occup Ther Pediatr*. 2023 Jan 10:1-20.

Skeletal maturation and long-bone growth patterns of patients with Progeria: a retrospective study. Tsai et al., *The Lancet. Child and Adolescent Health*. 2020 Apr;4(4):281-289.

Extraskeletal Calcifications in Hutchinson-Gilford Progeria Syndrome. Gordon et al., *Bone*. 2019 Aug;125:103-111.

Craniofacial Abnormalities in Hutchinson-Gilford Progeria Syndrome. Ullrich et al., *American Journal of Neuroradiology*. 2012 Sep;33(8):1512-8.

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.

Hutchinson-Gilford progeria is a skeletal dysplasia. Gordon, et al., *Journal of Bone and Mineral Research*. 2011 Jul;26(7):1670-9.

Ophthalmology:

Ophthalmologic Features of Progeria. Mantagos et al., *American Journal of Ophthalmology,* 2017 Oct;182:126-132.

Audiology:

Otologic and Audiologic Manifestations of Hutchinson-Gilford Progeria Syndrome. Guardiani et al., *The Laryngscope*, 2011, 121(10): 2250-2255.

PRF Granting Structure

PRF's research focus is highly translational. Topics must fall within the following research priorities:

- Projects that are likely to lead to clinical treatment trials within 5 years. This includes the discovery and/or testing of candidate treatment compounds in cell-based or animal models of HGPS. Only proposals that test compounds in a progerin-producing animal or cell model will normally be considered. Analyses in non progerin-producing models are acceptable, but only as a comparison to progerin-producing models and with strong justification.
- Development of gene-and cell-based therapies to treat Progeria
- Assessment of natural history of disease that may be important to developing outcome measures in treatment trials (preclinical or clinical)

Phase I Proposals: Awards are typically for 1-2 years in the range of $75,000/year. PRF will conduct a thorough cost analysis for each project during evaluations of submissions.

Required Qualifications. Principal investigators must hold a faculty appointment or equivalent. Awards will be granted only to applicants affiliated with institutions with 501(c)3 tax-exempt status, or the equivalent for foreign institutions.

Letter of Intent (LOI). A letter of intent is required and must be approved before a full application will be considered. Instructions to submit a Letter of Intent and grant application information, can be found at https://www.progeriaresearch.org/grant-application/.

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF Medical Research Committee

Volunteer MRC Reviews Grant Applications Semi-annually

In person left to right: Bob Bishop, Thomas Glover, Vicente Andres, Leslie Gordon, Christine Harling-Berg, Bryan Toole, Maria Eriksson, Ted Brown Virtually: Judith Campisi, Tom Mistelli

PRF Granting Structure

PRF's research focus is highly translational. Topics must fall within the following research priorities:

- Projects that are likely to lead to clinical treatment trials within 5 years. This includes the discovery and/or testing of candidate treatment compounds in cell-based or animal models of HGPS. Only proposals that test compounds in a progerin-producing animal or cell model will normally be considered. Analyses in non progerin-producing models are acceptable, but only as a comparison to progerin-producing models and with strong justification.
- Development of gene-and cell-based therapies to treat Progeria
- Assessment of natural history of disease that may be important to developing outcome measures in treatment trials (preclinical or clinical)

Phase I Proposals: Awards are typically for 1-2 years in the range of $75,000/year. PRF will conduct a thorough cost analysis for each project during evaluations of submissions.

Required Qualifications. Principal investigators must hold a faculty appointment or equivalent. Awards will be granted only to applicants affiliated with institutions with 501(c)3 tax-exempt status, or the equivalent for foreign institutions.

Letter of Intent (LOI). A letter of intent is required and must be approved before a full application will be considered. Instructions to submit a Letter of Intent and grant application information, can be found at https://www.progeriaresearch.org/grant-application/.

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Grant Funding Topics

As of December 31, 2023:

- Since inception **281** grant application received and **84** funded
- PRF has funded **69** principal investigators from **55** institutions in **14** countries

- Lamina A, progerin, Lamin B in HGPS and aging
- Genetics and nuclear function
- Preclinical Drug Therapy
- Molecular Abnormalities and Therapies
- Vascular Pathology
- Mouse Models
- Stem Cell Investigations and Therapy
- Clinical Trials

* Submissions include Letters of Intent and Full Grants

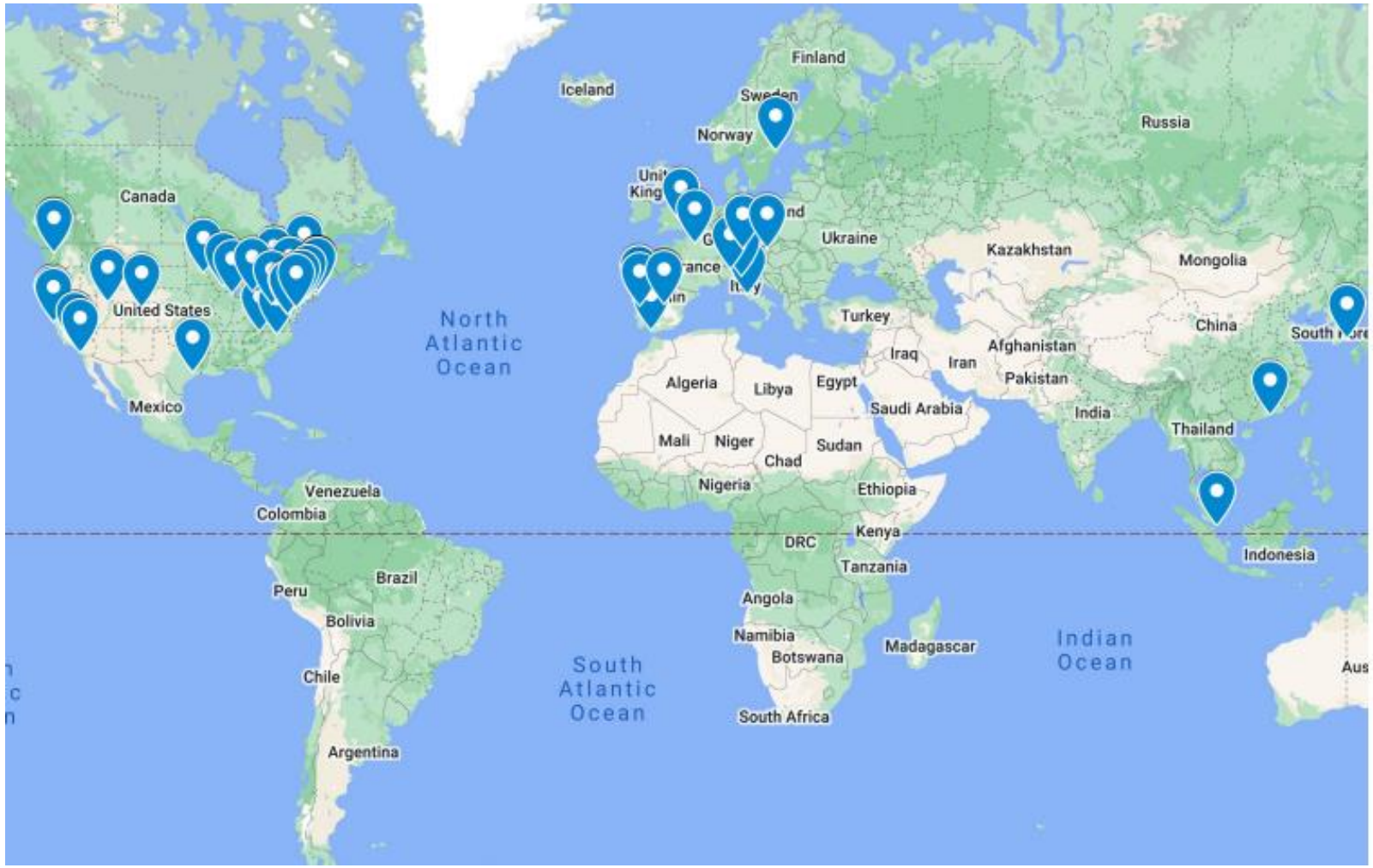
Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF Grantees

PRF has funded **69** principal investigators from **55** institutions in **14** countries

Complete list of Grantees available at:

https://www.progeriaresearch.org/grants-funded/



Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

PRF Scientific Meetings

Meeting Goals:

- To promote collaboration between basic and clinical scientists toward progress in Progeria, cardiovascular, and aging research PRF has held international scientific meetings.

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

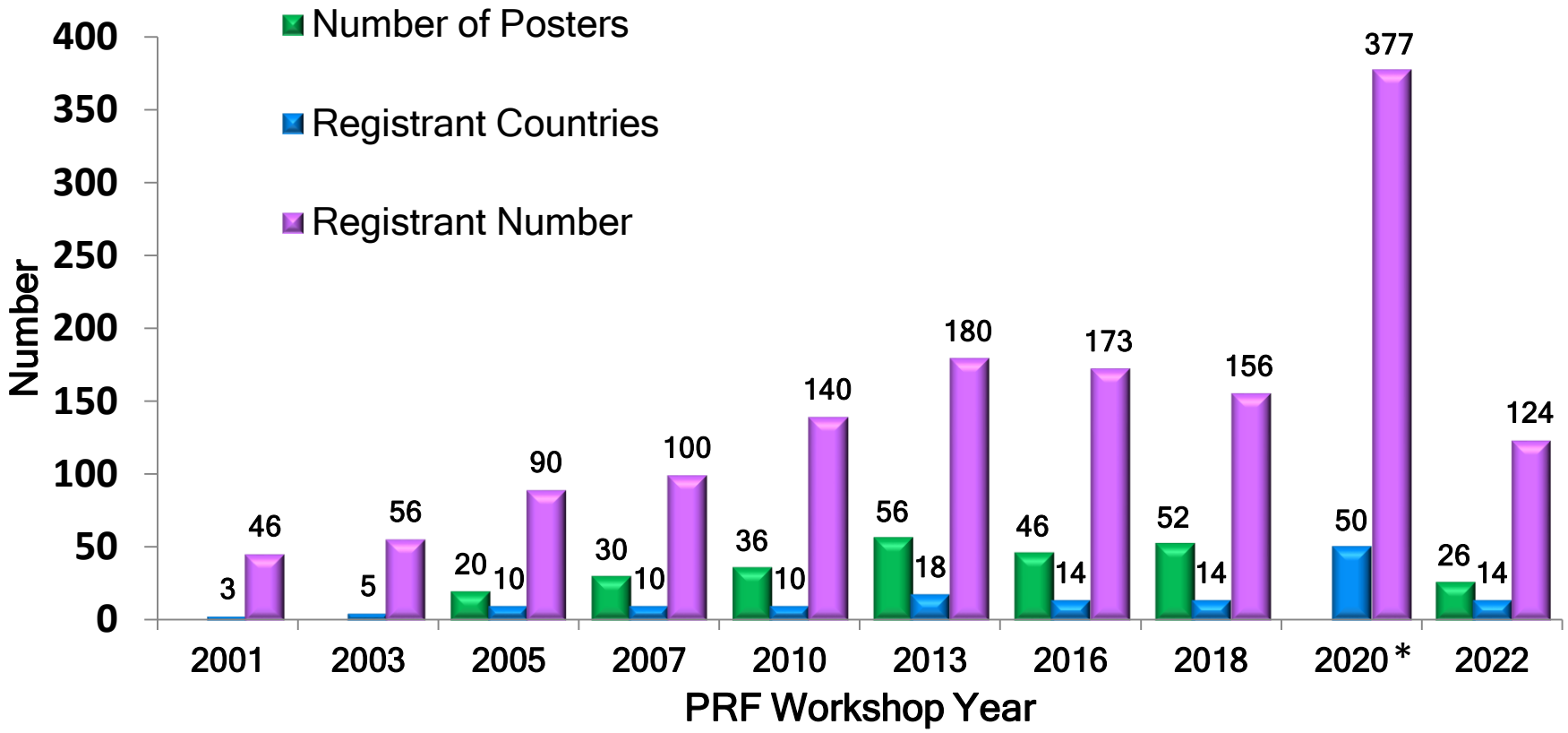
International Workshops Promoting Global Interest In Progeria, Cardiovascular Disease And Aging

These are large multi-day workshops open to all scientists. Clinical and basic researchers spend intense days sharing data and planning new collaborations for progress towards treatments and cure.

Various NIH Institutes have funded all international workshops through R13 and other granting mechanisms

Other organizations have also generously sponsored workshops

Growth of Global Interest In PRF Workshops



* 2020 was a webinar. Posters N/A

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Subspecialty Scientific Meetings

Small, focused meetings designed to promote and support work in areas of high interest for Progeria

- First Genetics Consortium Meeting – "Searching for the Progeria Gene", August 23, 2002, Brown University, Providence, RI
- Second Genetics Consortium Meeting – "Post- gene Discovery", July 30, 2003, Bethesda, MD
- Bone Marrow Transplant Meeting – "Forging Ahead by Exploring Potential Treatments", April 25-26, 2004, National Institutes of Health, Bethesda, MD
- New Frontiers in Progeria Research (2012), Boston, MA
- The first "Progeria Aortic Stenosis Intervention Summit", May 2, 2023, Virtual by Zoom

NIH National Heart, Lung, and Blood Institute

NIH National Human Genome Research Institute

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Scientific Publications

As of December 22, 2023:

185 Scientific articles have been published citing The Progeria Research Foundation Grants Funding Program

130 Scientific articles have been published citing PRF Cell & Tissue Bank resources:

- Publication list at www.progeriaresearch.org/prf-cell-and-tissue-bank-publications/

33 Scientific articles have been published citing The PRF Medical & Research Database:

- Publication list at www.progeriaresearch.org/medical-database/

28 Scientific articles have been published from clinical trial data

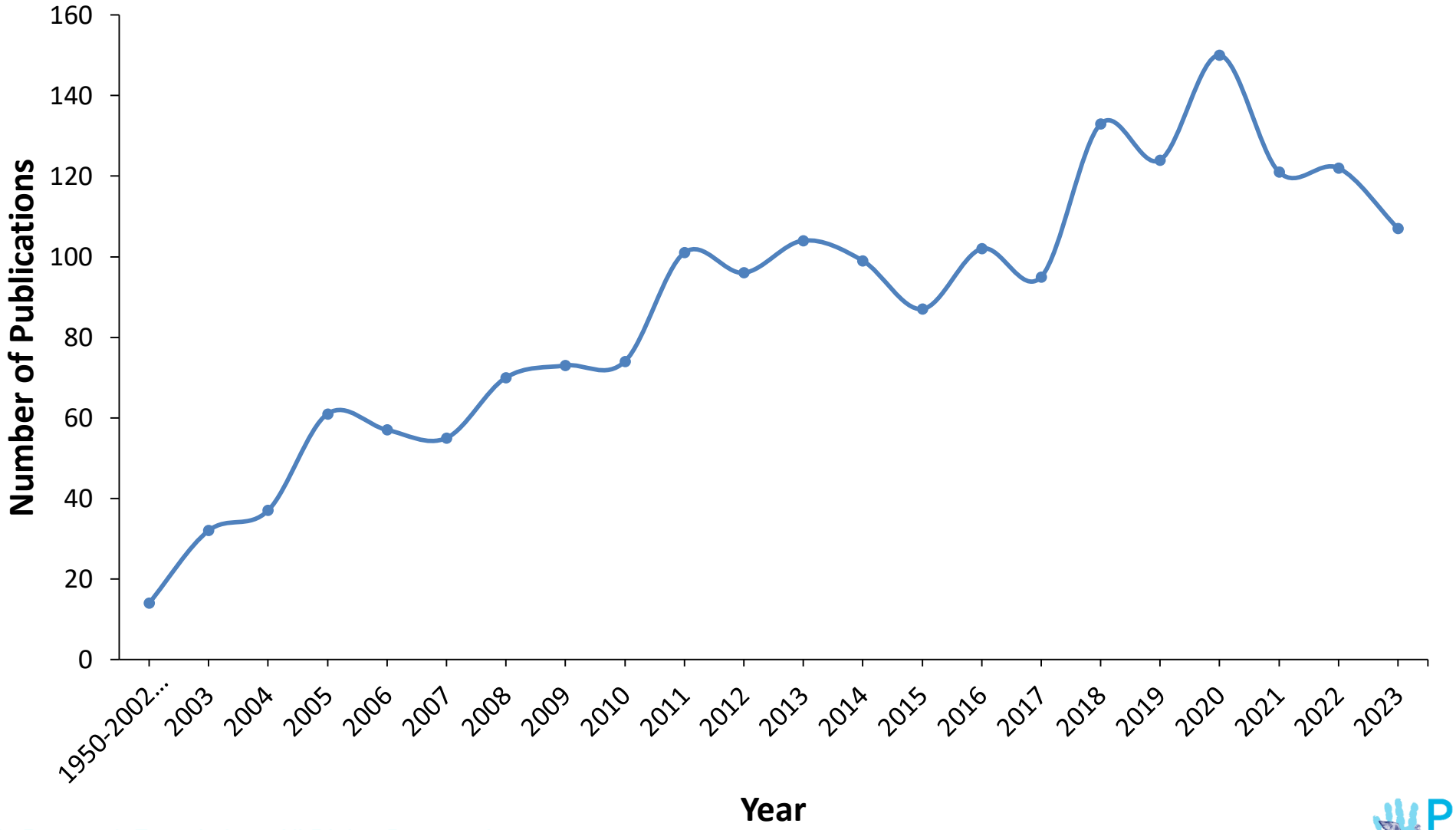
- See slide #54 and #55

4 Scientific articles have been published concerning PRF Scientific Workshops

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Progeria Related Publications

Today over 100 publications on Progeria a year are published in well-known, respected scientific journals read by researchers worldwide.

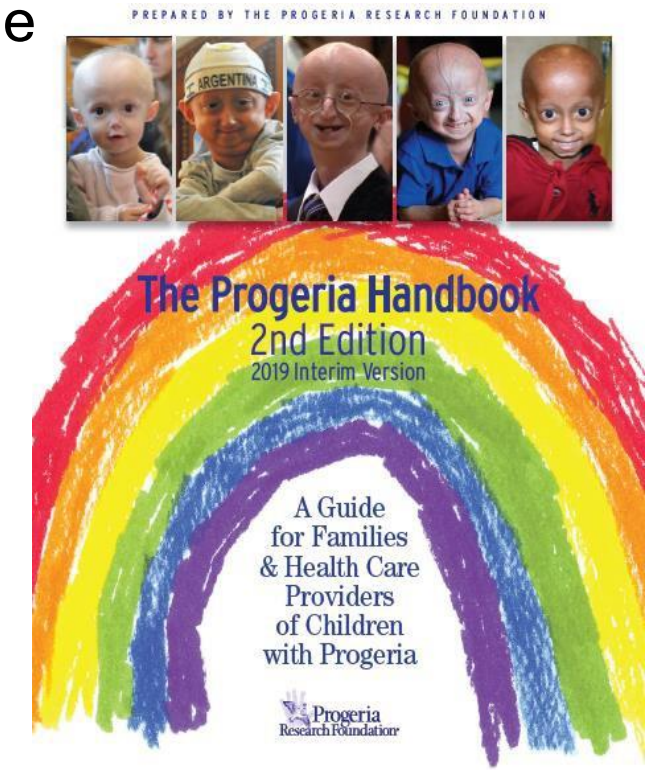


December 31, 2023

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Progeria Clinical Care Handbook

The Progeria Handbook 2nd Edition. A Guide for Families & Health Care Providers of Children with Progeria. *The Progeria Research Foundation.* Leslie B. Gordon MD, PhD; Medical Director (editor) 2019.



- Provided in Chinese, English, Italian, Japanese, Portuguese and Spanish
- Expert contributors from Boston Children's Hospital
- Number of Progeria Care Handbooks distributed to families of those with Progeria and their care givers: **921**

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

The Progeria Research Foundation

Finding…
Diagnosing…
Studying…
Treating…
CURING

Progeria Research Foundation
FOR THE CHILDREN ♥ FOR THE CURE

Together We *WILL* Find The Cure!

www.progeriaresearch.org