

# PRF By The Numbers



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

# Table of Contents

● Introduction and Collaborations	3 - 10
● Overview Data	11 -20
● International Progeria Registry	21 - 24
● PRF Diagnostics Program	25 - 28
● PRF Cell & Tissue Bank	29 - 35
● PRF Medical & Research Database	36 - 40
● Weighing - In Program	41 - 44
● Clinical Trials	45 - 55
● Progerin Biomarker	56 - 58
● PRF Grants Program	59 - 63
● Scientific Meetings and Workshops	64 - 67
● Publications	68 - 71

# 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.

# 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.



# 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

# 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

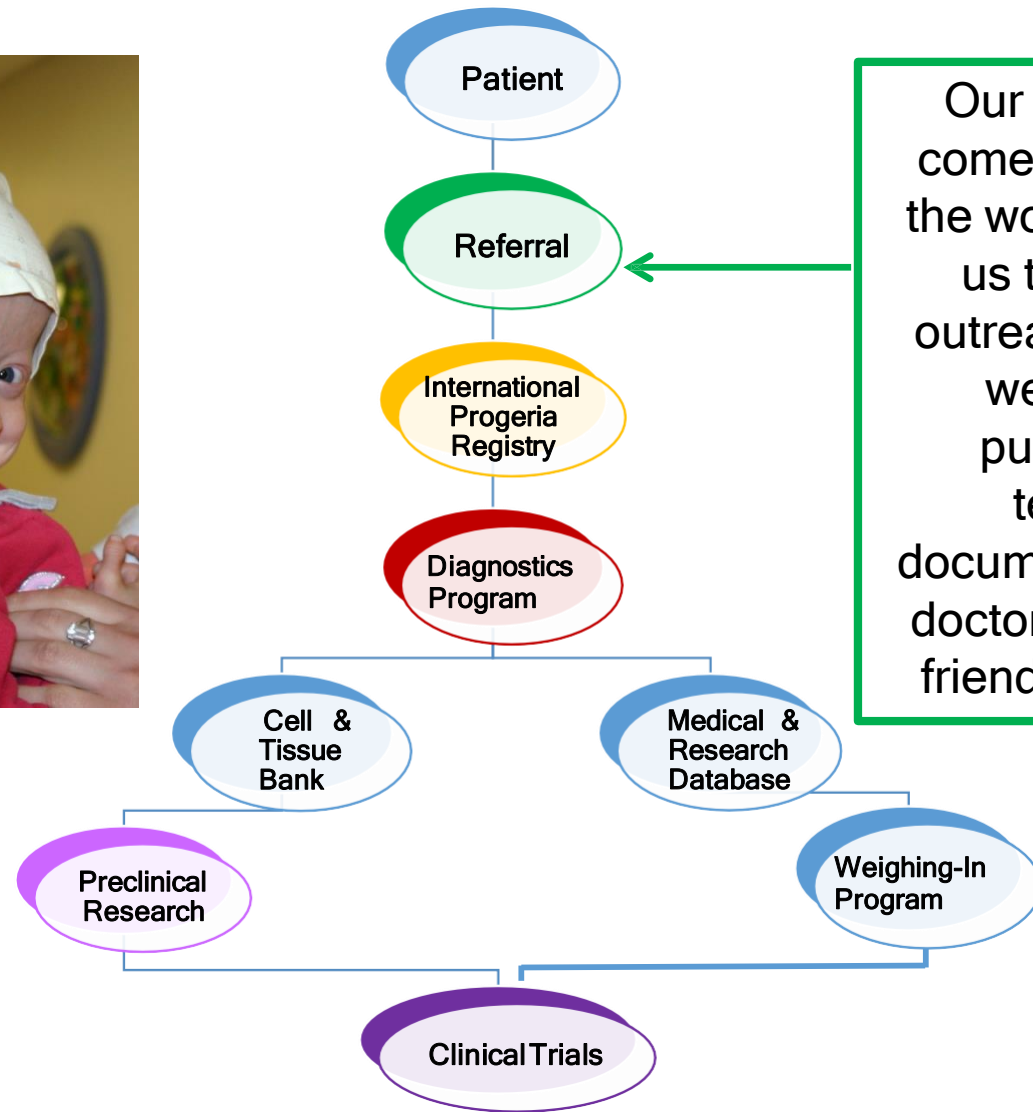
Physicians

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

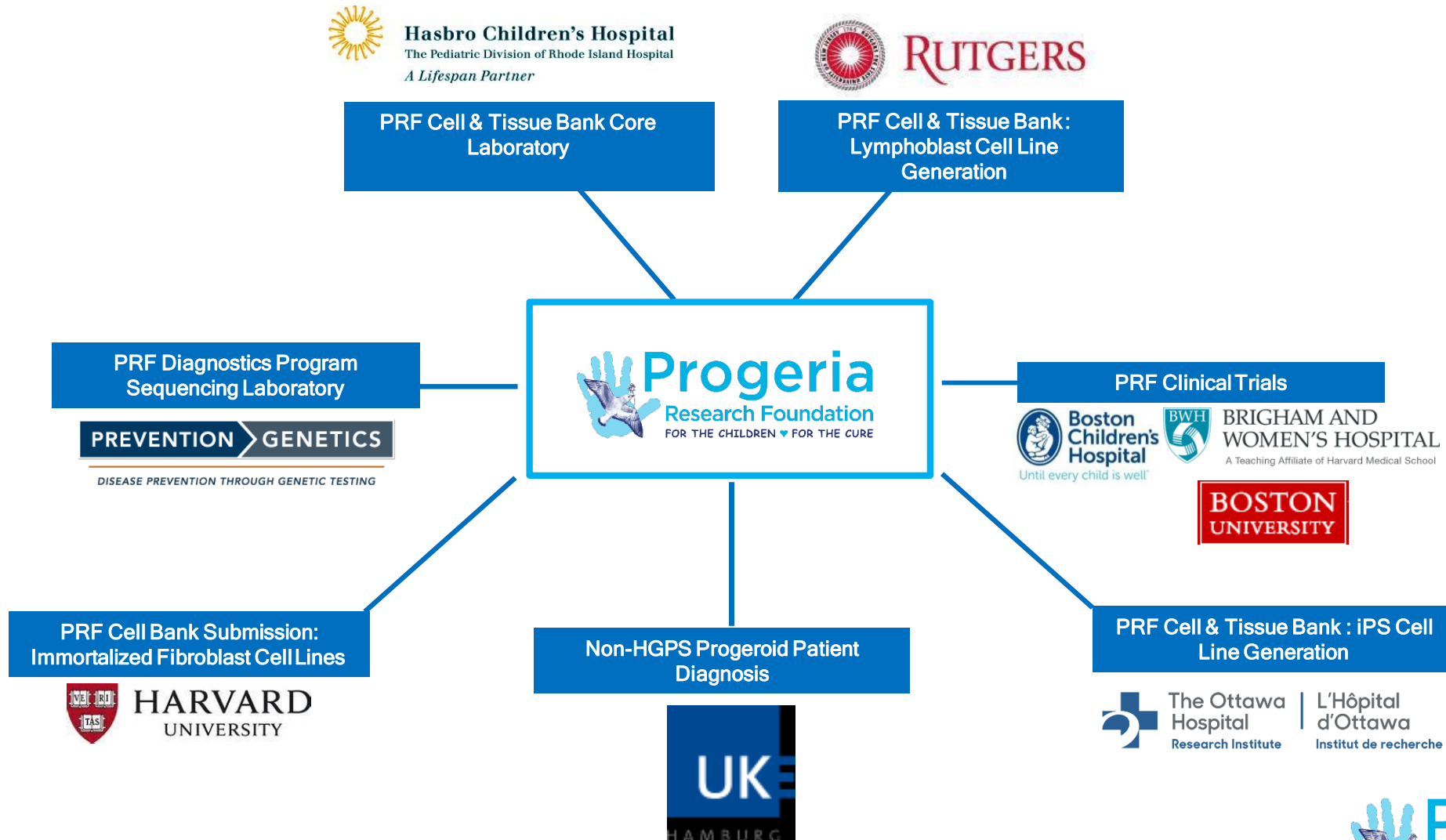
[info@progeriaresearch.org](mailto:info@progeriaresearch.org)

# 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.


# 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

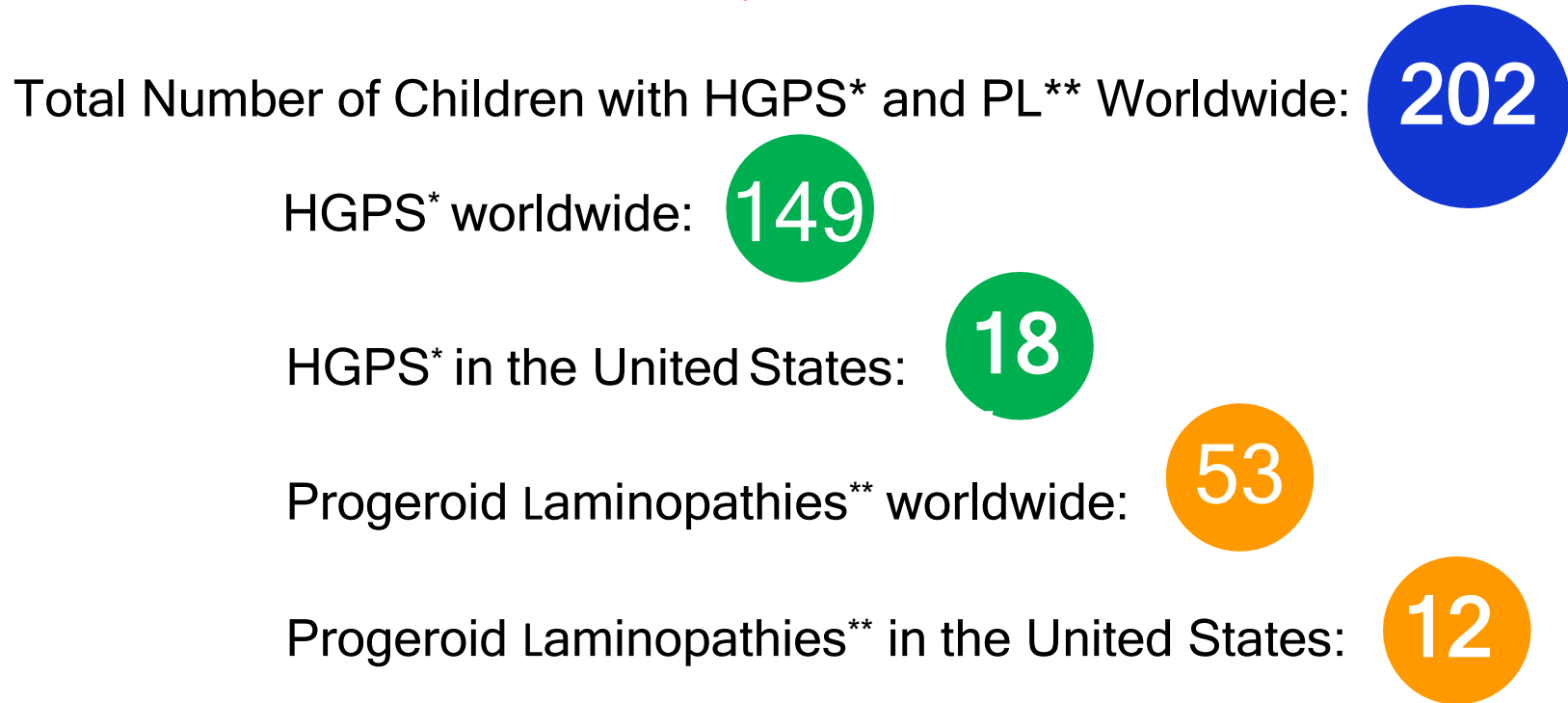


NIH - funded Clinical and Translational Study Unit at Boston Children's Hospital



# Number of Living PRF-Identified Cases

March 31, 2024



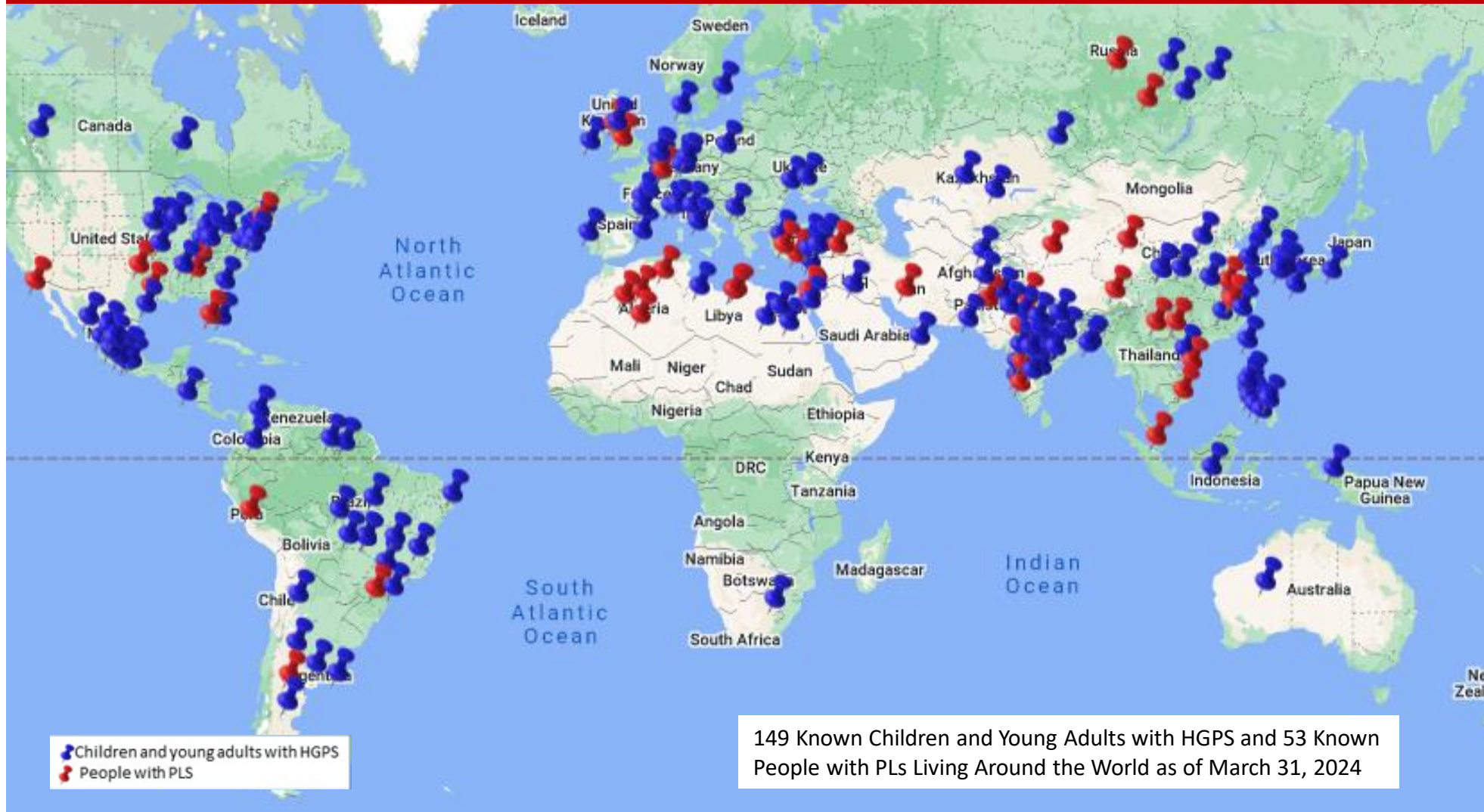
\*Children in the HGPS category have a progerin-producing mutation in the LMNA gene

\*\*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

# PRF-Identified People Living with HGPS & PL Reside In 51 Countries

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



Libya  
 Luxembourg  
 Malaysia  
 Mexico  
 Nepal  
 Netherlands  
 Oman  
 Pakistan  
 Palestine-Gaza  
 Papua New Guinea  
 Peru  
 Philippines  
 Poland  
 Portugal  
 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 35 Languages

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

прогерии исследовательский фонд

خطيشلا ناحباً تفسؤم

早衰症研究基金會

Progeria रिसिच फाउंडेशन



조로증 연구 재단

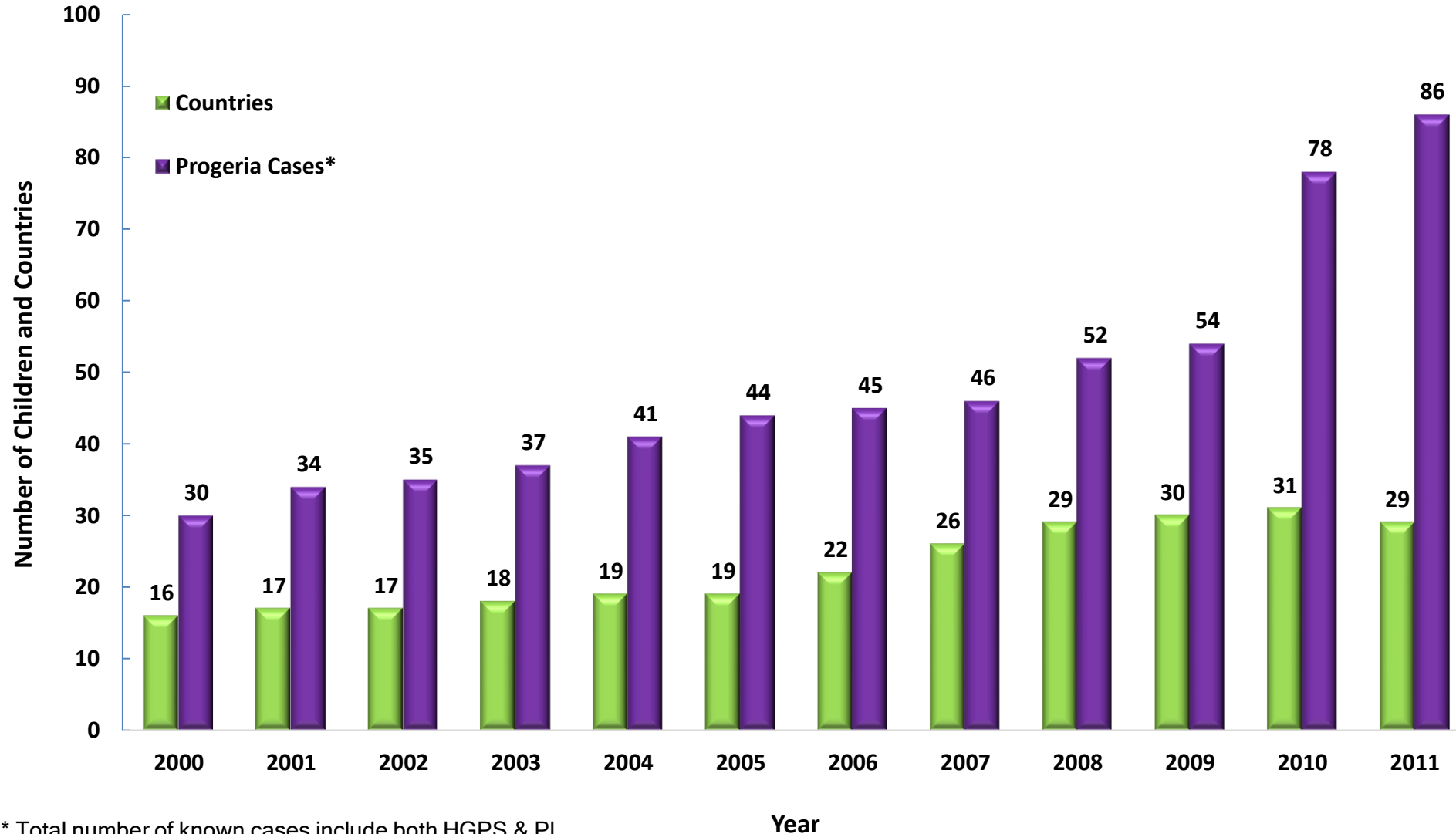
Progeria Araştırma Vakfı

早老症研究財団

ಬಾಲ್ಯದ ಬಾಲ್ಯಕ್ಕೆ ವಯಸ್ಸು ಸಮುದರುಕಂಡು ನನ್ನ ವೃದ್ಧಿ-ಪ್ರಯತ್ನಗಳನ್ನು  
ವರ್ಧಿಸಲು ಸಹಾಯ ಮಾಡಿ

# Every Year Our Numbers Grow

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

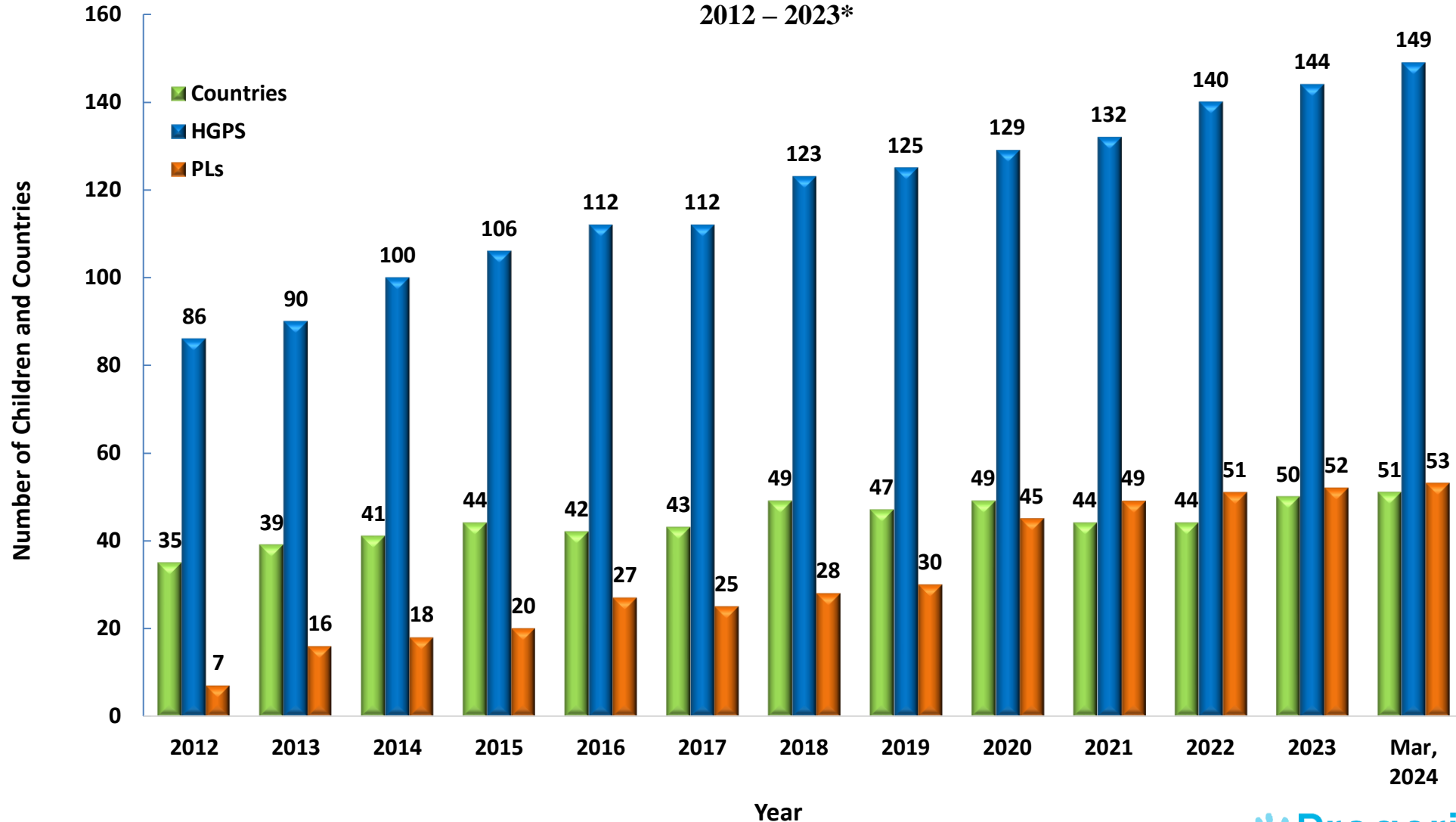


\* Total number of known cases include both HGPS & PL

\* When a child passes away, numbers are decreased

# Every Year Our Numbers Grow

Living Children and Adults PRF has identified with Progeria and PLs and the countries they reside in from 2012 – 2023\*



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

# 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.



# 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


March 31, 2024 population statistics:

 The US population is:

**341,268,484 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.

# Prevalence and World Population of Progeria

Given the world population on March 31, 2024

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

# 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 March 31, 2024:



Brazil's population was estimated as

**217,272,431** people



Using Prevalence, the number of children living with Progeria in Brazil is  $217,272,431 / 19,000,000 =$

**11**



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



\* Data based on the latest *Worldometers* estimates

# International Progeria Registry\*

## Program Goals:

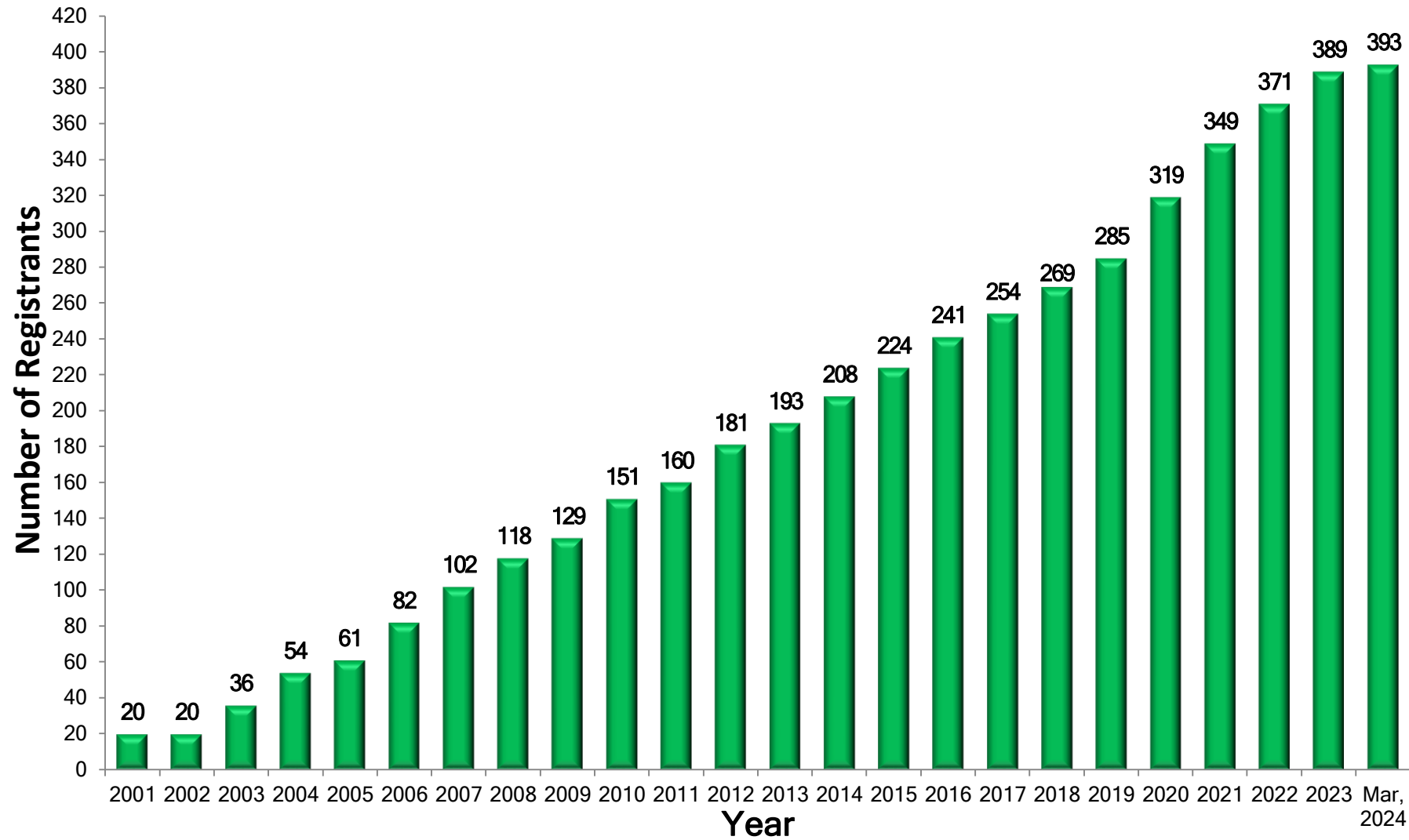
- Patient identification
- Outreach to patient families and their physicians
- A springboard for program enrollment

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

# 393 Children and Adults Have Been Registered With PRF



# From 72 Countries and 1 Territory

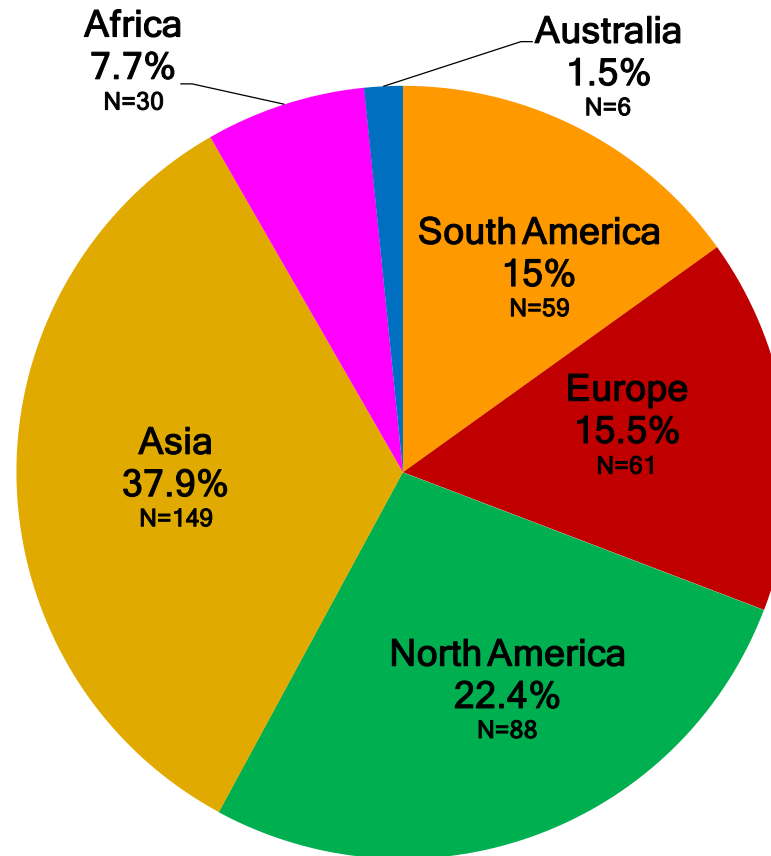


Algeria  
Argentina  
Australia  
Bangladesh  
Belgium, Bolivia  
Brazil, Bulgaria  
Canada, Chile  
China, Colombia  
Czech Republic  
Denmark  
Dominican Republic  
Ecuador, Egypt  
England, Ethiopia,  
Finland  
France, Germany  
Guatemala, Guyana  
Honduras  
Hong Kong  
India, Indonesia  
Iran,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

# ...And All Continents

Participation (%) By Continent





# PRF Diagnostics Program

## Program Goal:

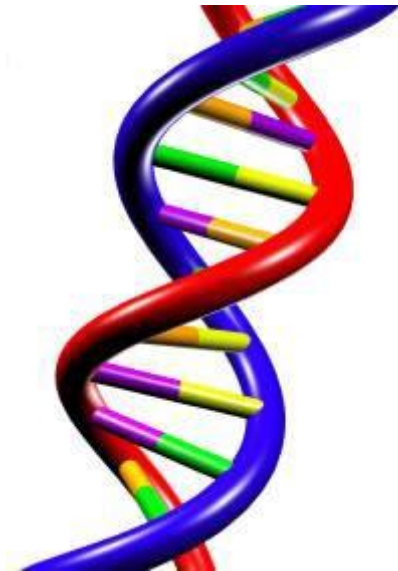
- Genetic Sequence Testing for Progeria-causing mutations

## 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/>



# Diagnostics Testing Summary

March 31, 2024

Total Number of Proband Tests Performed:

170

Exon 11 (HGPS) Mutations:

117

Other Progeroid Laminopathies (Exons 1 - 12):

13

ZMPSTE24 Mutations :

2

Average Number of Patients Tested Per Year :

8

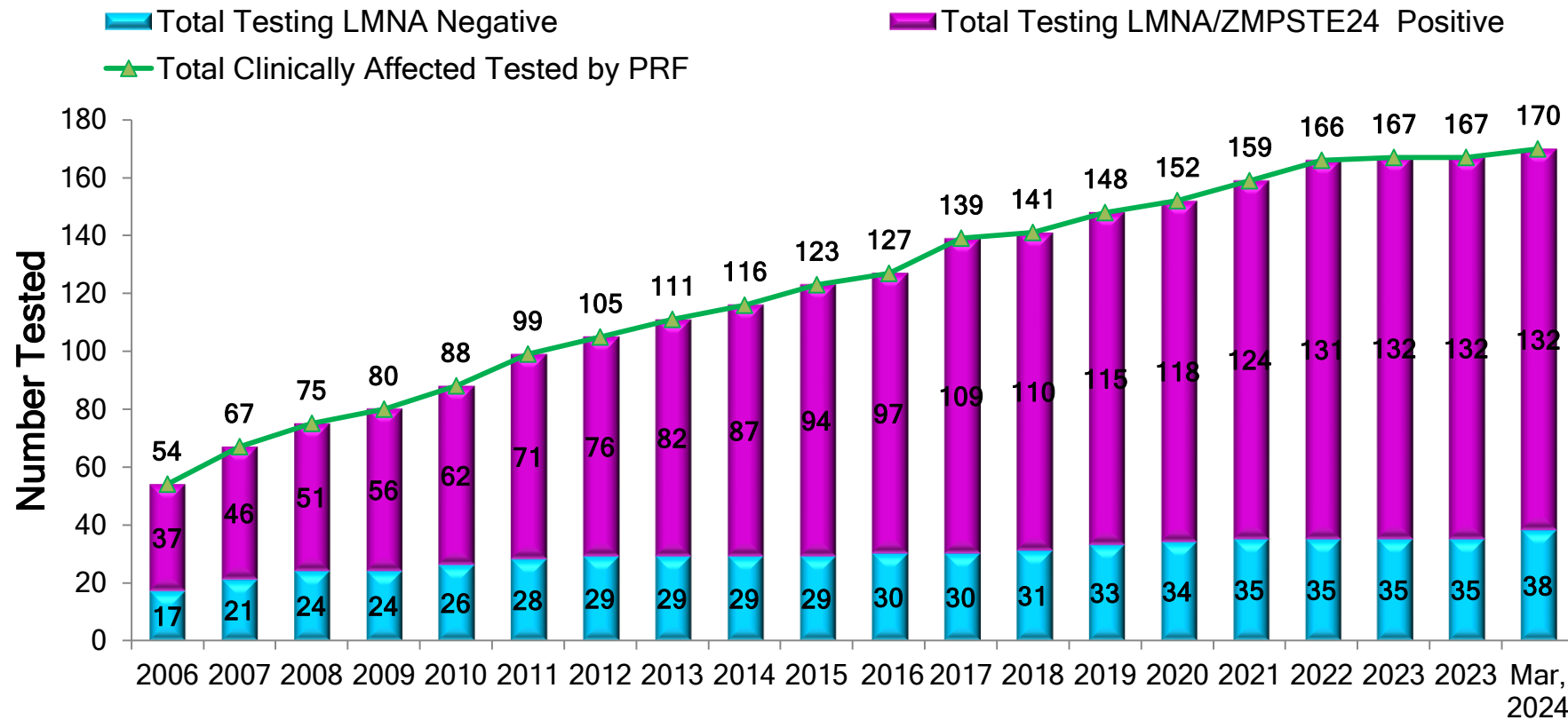
All tests are performed in a Clinical Laboratory Improvement Amendments (CLIA) certified facility.

# Mutations Identified Through PRF Diagnostics Program

DNA Mutation	Amino Acid Effect	Zygoty	Progerin Producing?	Number Diagnosed
<b>Classic HGPS - LMNA Mutation</b>				
1824 C>T, exon 11	G608G	heterozygous	Yes	103
<b>Non Classic HGPS- LMNA Mutation</b>				
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
<b>Progeroid Laminopathy- LMNA Mutation</b>				
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
<b>Progeroid Laminopathy- ZMPSTE2424 Mutation</b>				
1274T>C, exon 10	L425P	homozygous	No	2

# 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

# 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/>

# PRF Cell and Tissue Bank Holdings

As of March 31, 2024

Total Number of Participants:

383\*

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

# Mutations Available in PRF Cell & Tissue Bank

DNA Mutation	Amino Acid Effect	Zygoty	Progerin Producing?	Cell Type DFN=Dermal Fibroblast LBV= Lymphoblast
<b>Classic HGPS - LMNA Mutation</b>				
c.1824 C>T, exon 11	p.G608G	heterozygous	Yes	DFN, LBV, iPSC
<b>Non Classic HGPS- LMNA Mutation</b>				
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
<b>Progeroid Laminopathy- LMNA Mutation</b>				
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
<b>Progeroid Laminopathy- ZMPSTE2424 Mutation</b>				
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 March 31, 2024:

237

Research Teams From

29

Countries Have Received

1555 Cell Lines

204 DNA Samples

457 Tissue, plasma, serum  
and other biological samples

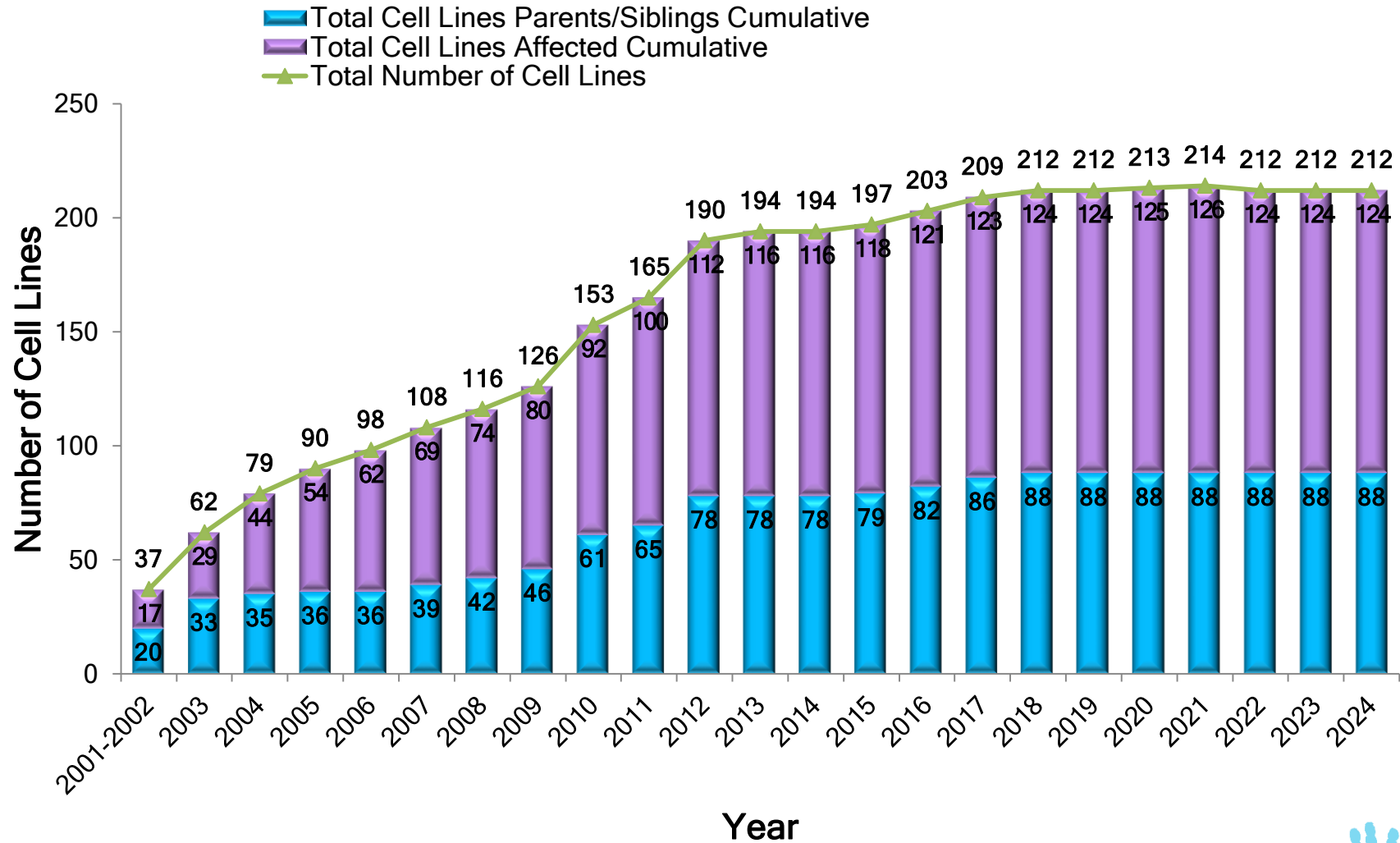
33 Lonafarnib Samples



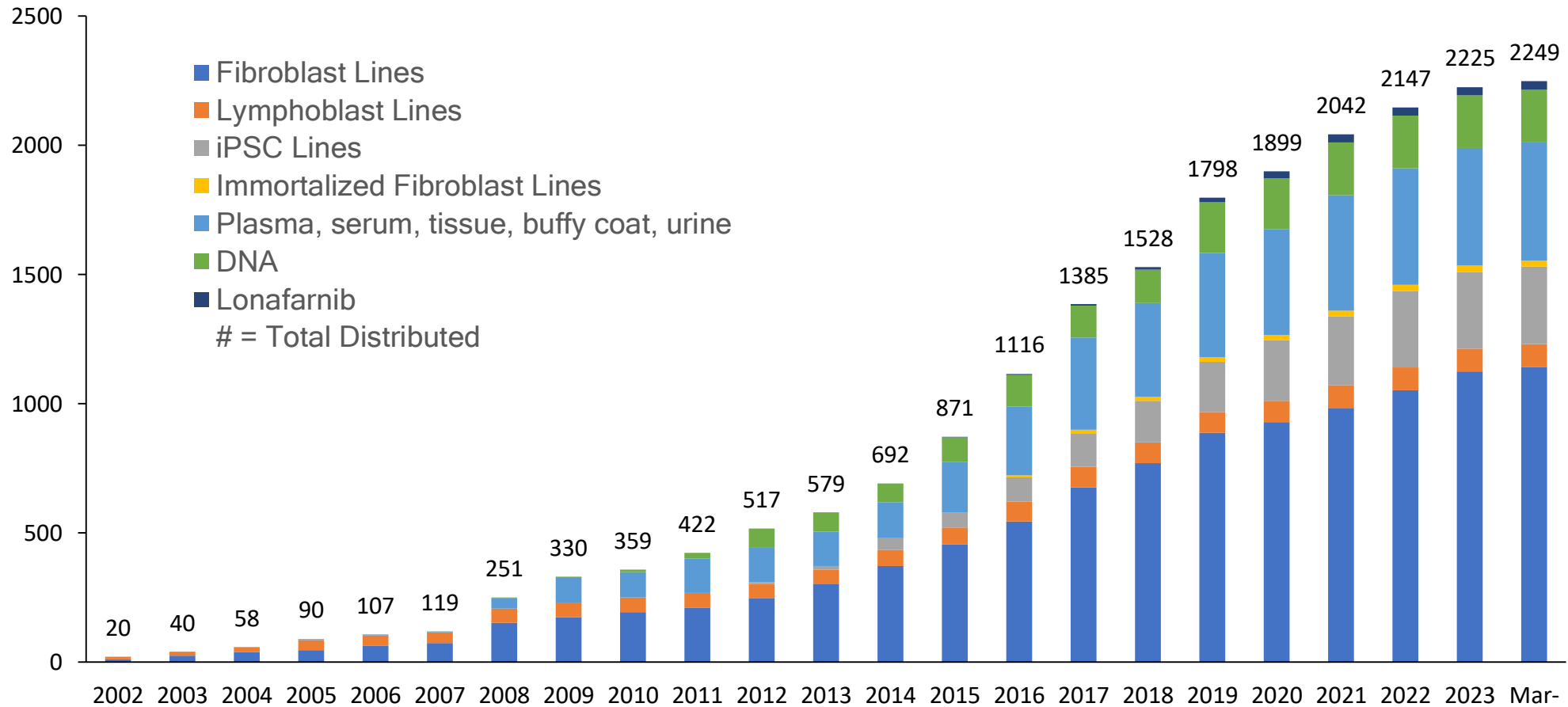
Senescent Progeria  
Fibroblasts in Culture



# Number Of Cell Lines By Year



# Cumulative Number of Biological Samples Distributed

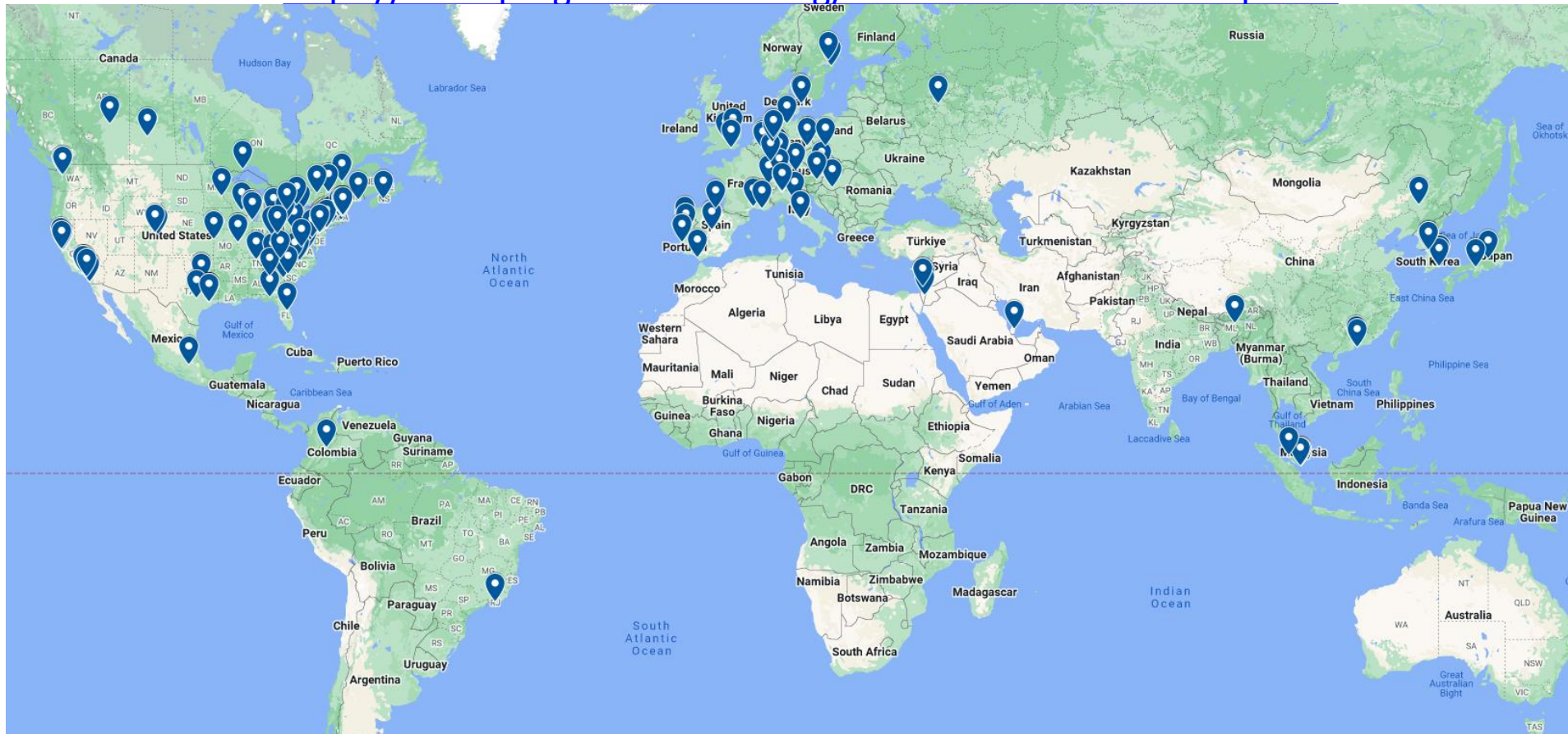


# Cell and Tissue Bank Recipients

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>



# 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



# 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/>

# Medical & Research Database Participation

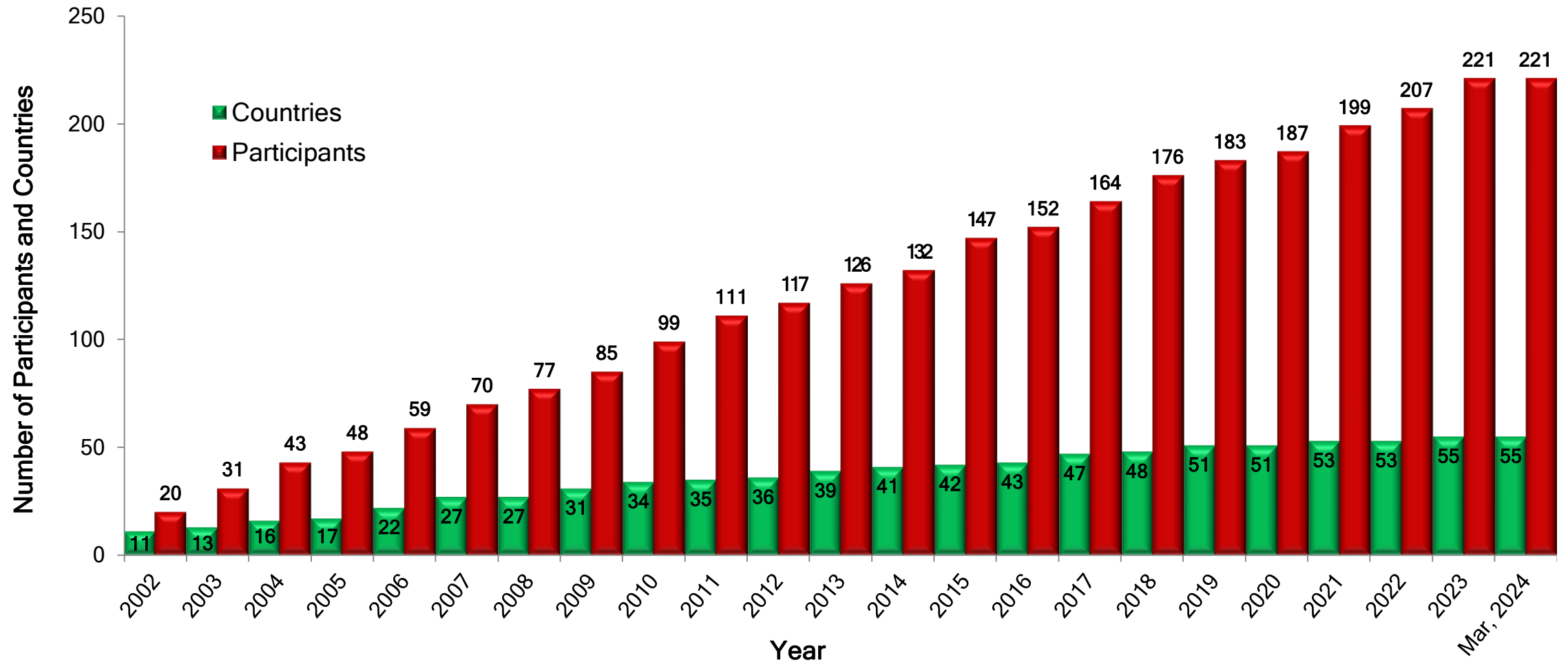
**221** Participants are enrolled from **55** countries and **1** US territory

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



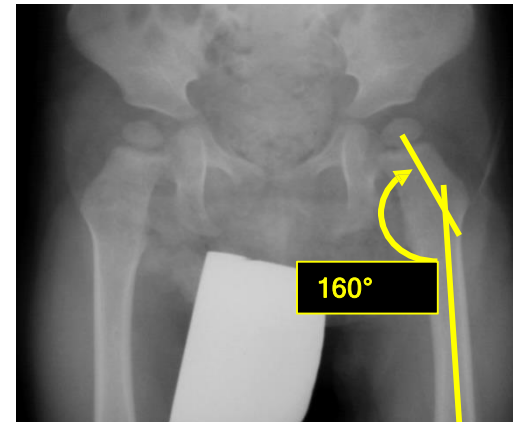
Libya, Mexico  
Morocco, Nepal  
Netherlands  
Oman, Pakistan  
Papua New Guinea  
Peru, Philippines  
Poland, Portugal  
Puerto Rico  
Romania, Russia  
Senegal, Serbia  
South Africa  
South Korea  
Spain, Sri Lanka  
Suriname, Sweden  
Tanzania, Togo  
Turkey, Ukraine  
USA, Venezuela  
Vietnam

# Medical & Research Database Longitudinal Enrollment



# Types Of Data Collected

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





# 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



# Weighing-In Program Participation

122

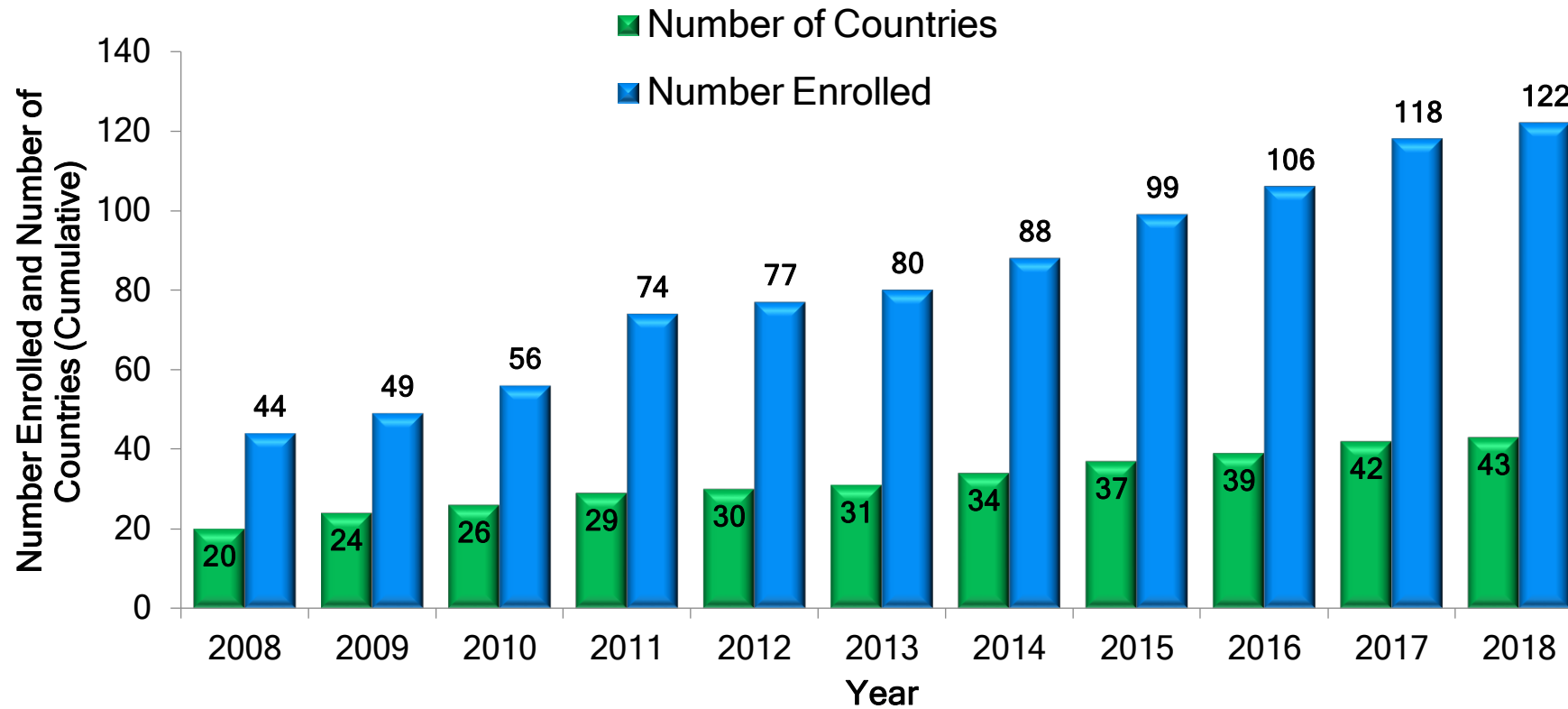
Participants are enrolled from **42** countries and **1** US territory

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



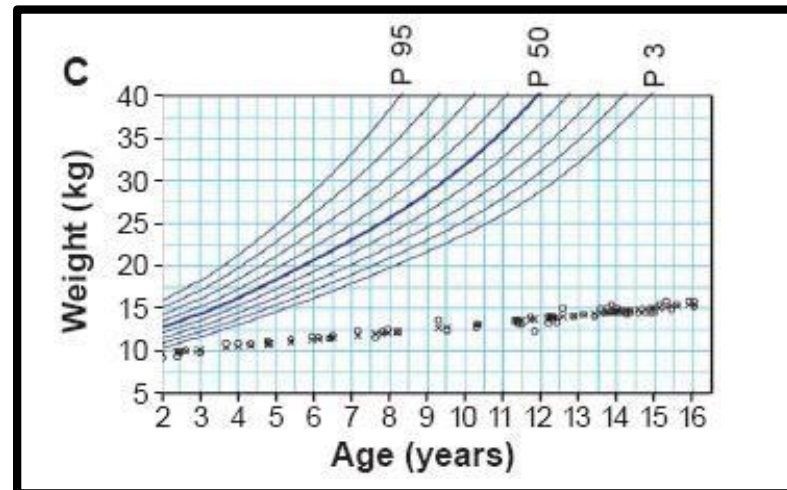
Nepal  
Pakistan  
Peru  
Philippines  
Poland  
Portugal  
Puerto Rico  
Romania  
Russia  
Senegal  
South Africa  
South Korea  
Spain  
Sri Lanka  
Togo  
Tanzania  
Turkey  
Ukraine  
USA  
Venezuela  
Vietnam

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



# 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

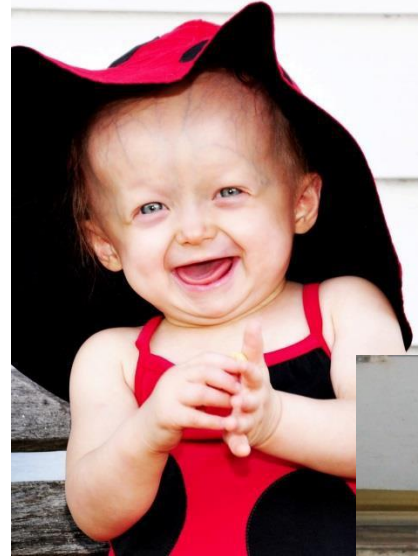
# PRF-Funded Clinical Treatment Trials



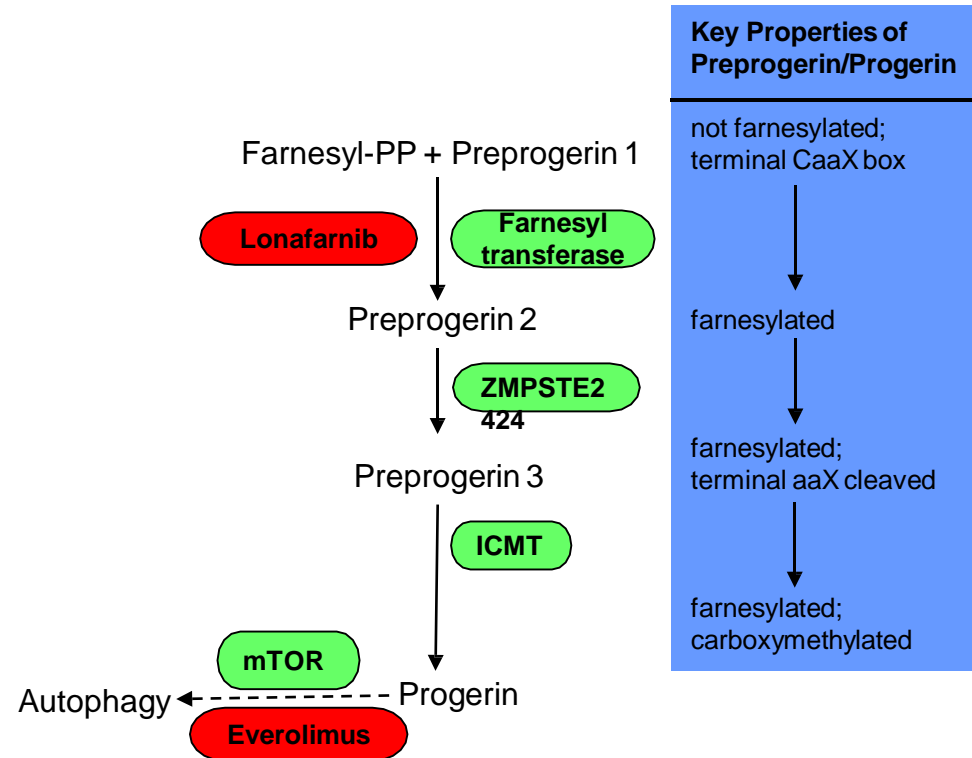
# Clinical Drug Treatment Trials

## 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



# 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.

# 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 March 31, 2024	





# Participation in PRF Clinical Trials

107

Children have participated in PRF Clinical Trials from 42 countries








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

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

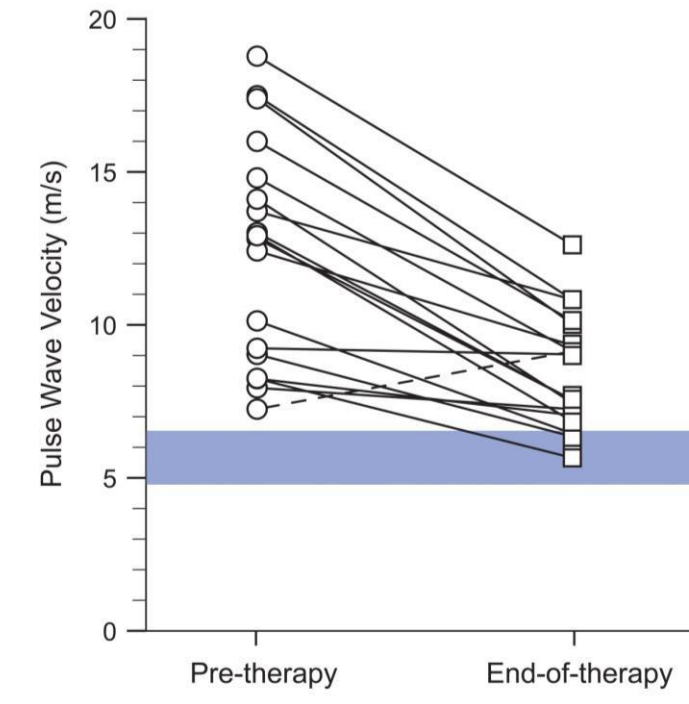
# Clinical Treatment Trial Efficacy Results

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

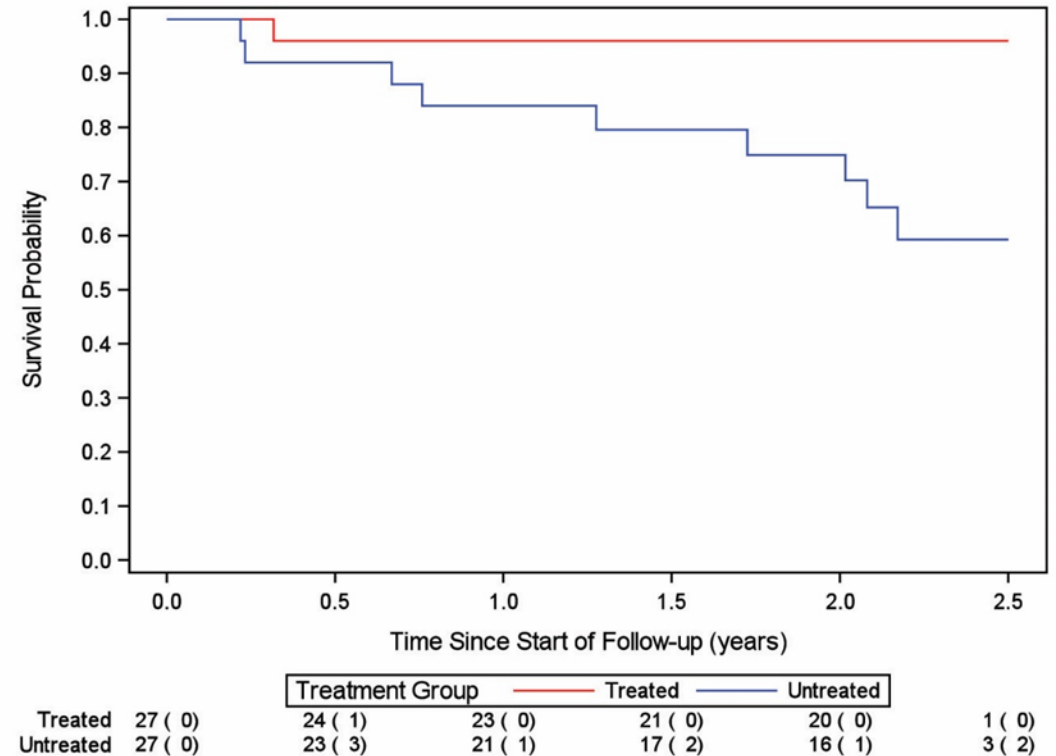
Gordon et al, PNAS, 2011



# 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](mailto:info@progeriaresearch.org) for more information on how to access Zokinvy (lonafarnib) for your child or patient with Progeria

# 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**



# 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:

Abnormal Myocardial Deformation Despite Normal Ejection Fraction in Hutchinson-Gilford Progeria Syndrome. Olsen, et al. *J Am Heart Assoc*. 2024;13(3)

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.

Extraskelatal 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 Laryngoscope*, 2011, 121(10): 2250-2255.

# Progerin as a Biomarker for Progeria



Progerin is the toxic protein produced by cells with progeria in place of the normal lamin A protein



Normal lamin A plays a role in cell division, but the toxic progerin gets stuck to the nuclear membrane of cells, and its accumulation causes progeria



A biomarker is “a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease” (National Cancer Institute)



Treatments for progeria aim to decrease the amount of progerin produced by the body.





# Publication of the Progerin Biomarker




research-article

Circulation

**ORIGINAL RESEARCH ARTICLE**



## Plasma Progerin in Patients With Hutchinson-Gilford Progeria Syndrome: Immunoassay Development and Clinical Evaluation

Leslie B. Gordon , MD, PhD; Wendy Norris, MS; Sarah Hamren, BS; Robert Goodson, BS; Jessica LeClair, PhD; Joseph Massaro, PhD; Asya Lyass, PhD; Ralph B. D'Agostino Sr, PhD; Kelsey Tuminelli, MS; Mark W. Kieran , MD, PhD; Monica E. Kleinman , MD



Dr. Gordon *et al.* 2023 developed an assay to measure progerin in blood plasma

# Further Findings of the Progerin Biomarker Study



Plasma progerin levels were 95x higher in those with progeria than in the average healthy human



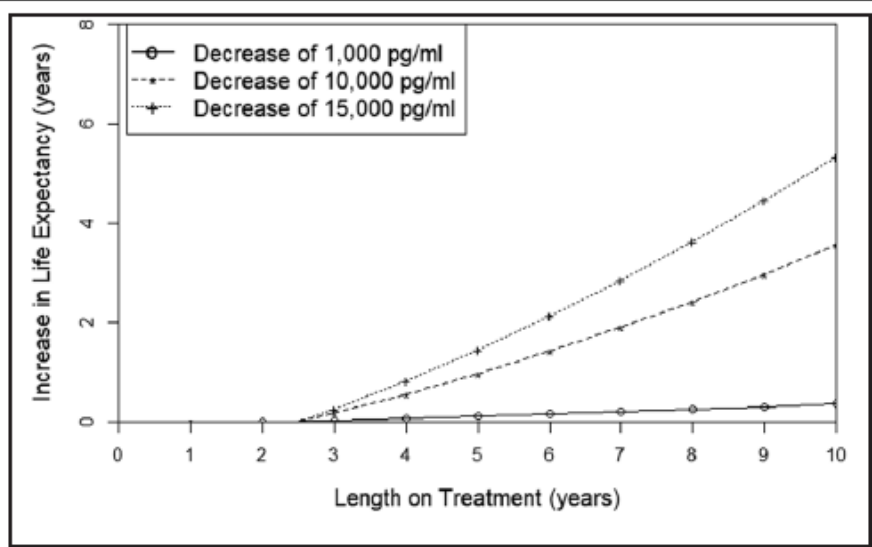
Treatment with lonafarnib decreased progerin levels by 35-62% on average



Lifespan increase was shown to be linked to decreased progerin levels and longer time on treatment



Long-term treatment with lonafarnib (10+ years) resulted in a lifespan increase of about 35%



Gordon *et al.* 2023, *Circulation*

# 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/>.

# 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

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# Grant Funding Topics

As of **March 31, 2024**:

- Since inception **281** grant application received and **85** 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



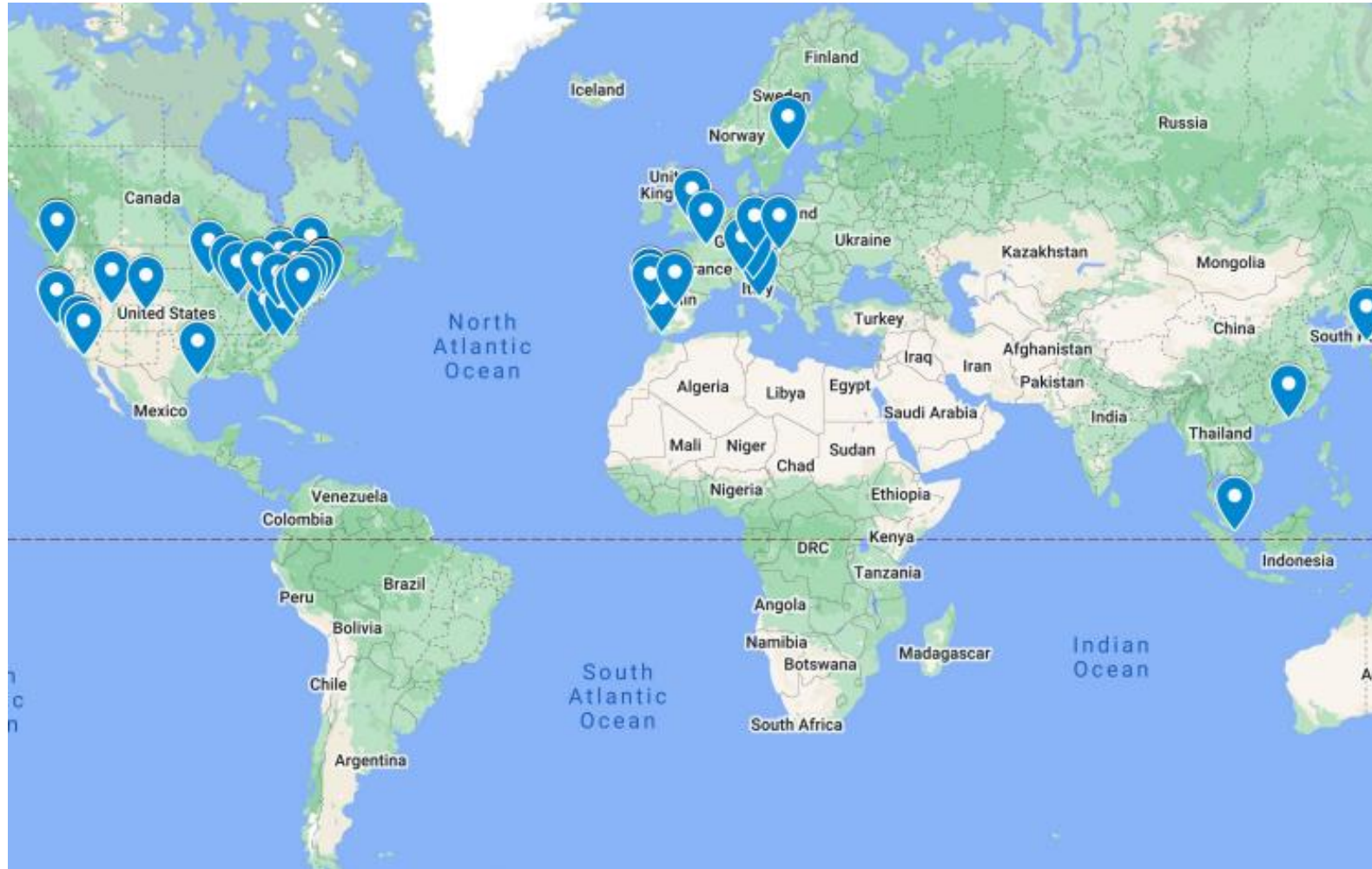
Clinical Trials

# 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/>



# 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.





# 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



The Max and Victoria Dreyfus Foundation, Inc.



Jack & Pauline Freeman Foundation, Inc.



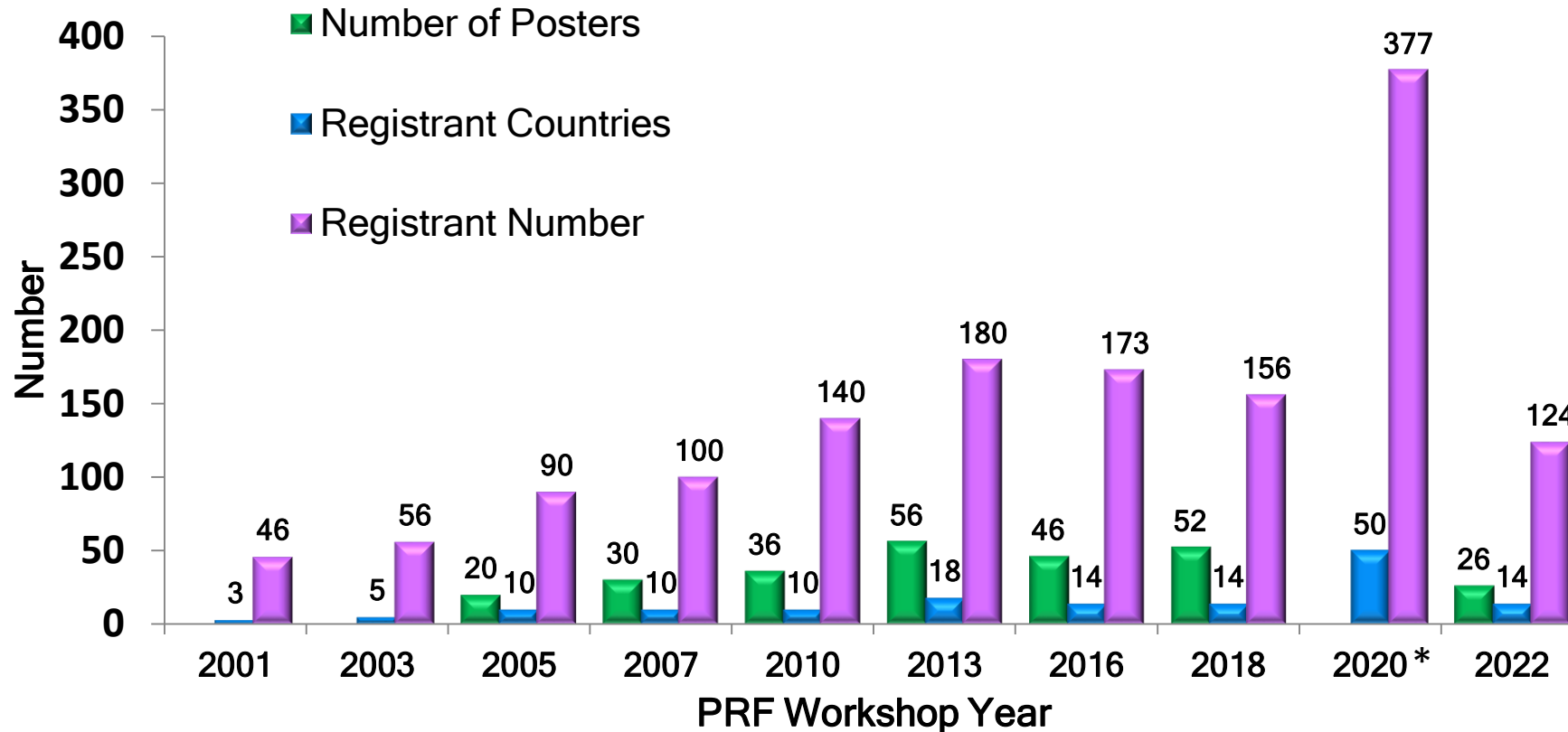
DSF Charitable Foundation



GLENN FOUNDATION FOR MEDICAL RESEARCH



# Growth of Global Interest In PRF Workshops



\* 2020 was a webinar. Posters N/A

# 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



# Scientific Publications

As of March 31, 2024:

187

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

131

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



[Publication list at www.progeriaresearch.org/prf-cell-and-tissue-bank-publications/](http://www.progeriaresearch.org/prf-cell-and-tissue-bank-publications/)

34

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



Publication list at [www.progeriaresearch.org/medical-database/](http://www.progeriaresearch.org/medical-database/)

29

Scientific articles have been published from clinical trial data



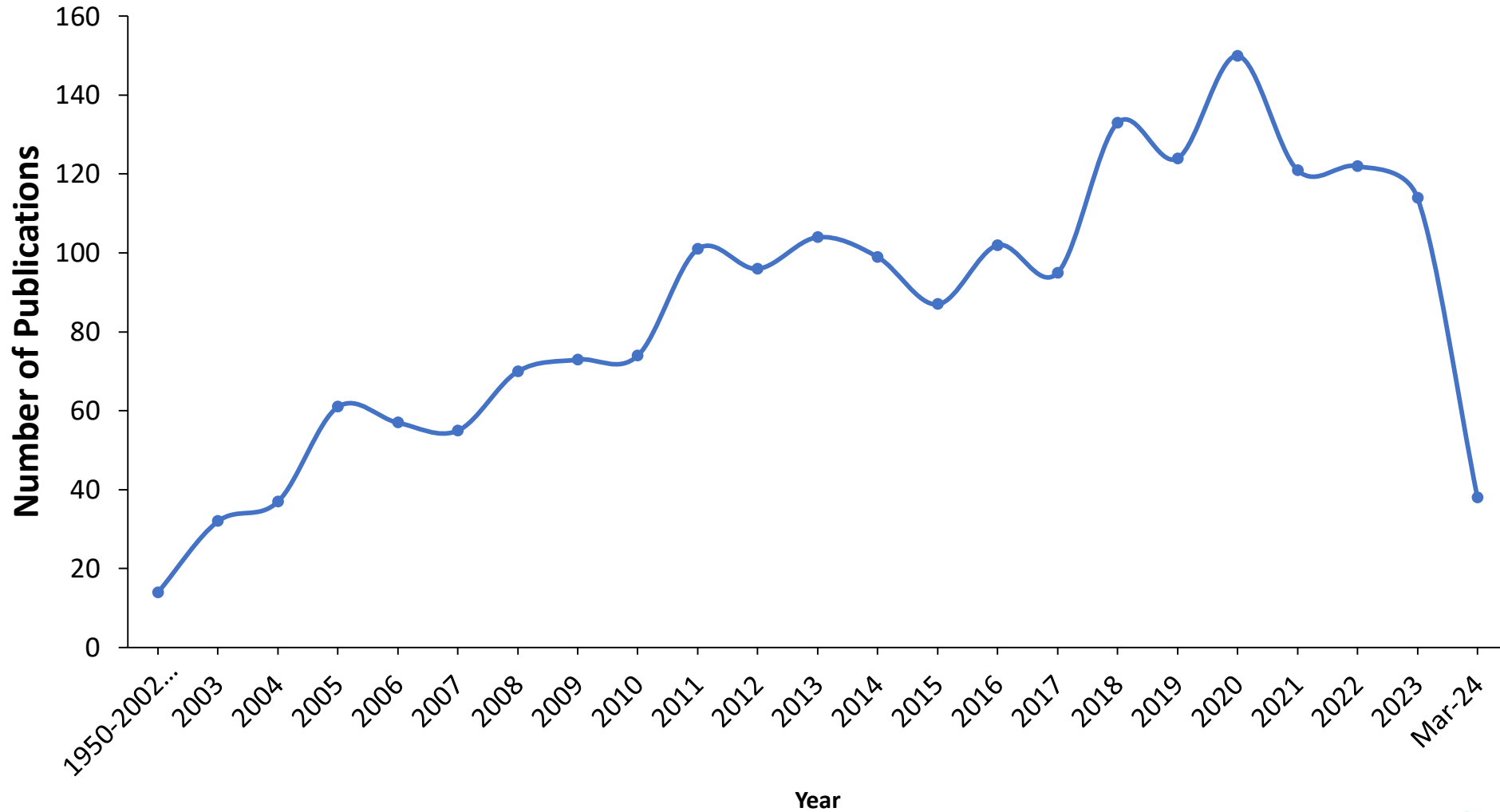
See slide #54 and #55

4

Scientific articles have been published concerning PRF Scientific Workshops

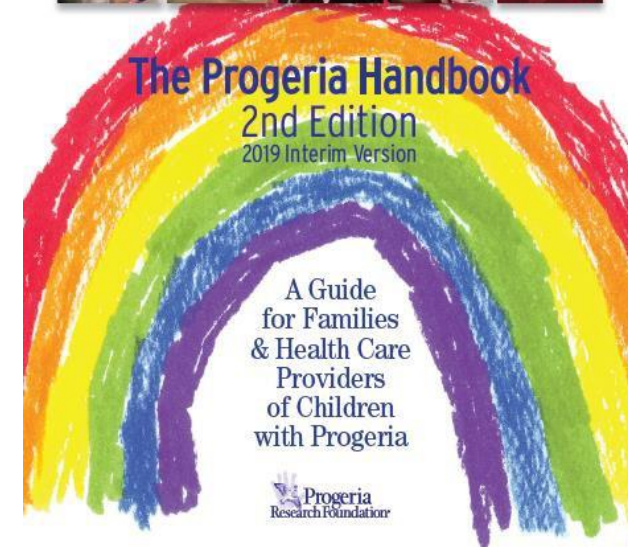
# Progeria Related Publications




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



# Progeria Clinical Care Handbook

The Progeria Handbook 2<sup>nd</sup> 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:

925

# The Progeria Research Foundation

Finding...  
Diagnosing...  
Studying...  
Treating...  
**CURING**



Together We *WILL* Find The Cure!

[www.progeriaresearch.org](http://www.progeriaresearch.org)