Progeria Research Foundation

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news

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We're a 4-Star Charity!
See page 12 for details

FANTASTIC NEWS! Drugs tested in PRF-funded clinical trials increase estimated lifespan of children with Progeria

In a stunning development, a first-ever study to assess whether treatments influence patient survival shows that the medications tested in the PRF-funded Boston-based Progeria clinical trials increased lifespan for children with Progeria.

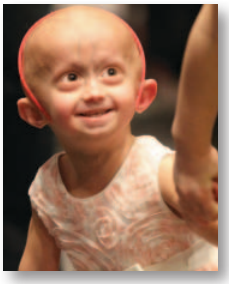
The study results reveal that children with Progeria receiving lonafarnib, along with two other drugs added in a later "triple therapy" study, had an 80 percent lower risk of death compared to the untreated group. Lonafarnib is the drug tested in the first-ever Progeria trial in 2007, and proved to be an effective treatment in several areas, including the critical cardiovascular system.

This is the first evidence of any treatments influencing survival for this fatal disease – an historic finding in our quest to improve health and extend the lives of children with Progeria.

See page 4 for details.

Cam, Zach and Miles love their trophies, awarded by PRF during their March visit to Boston Children's Hospital for completing the triple therapy trial.

See page 5 for the latest on clinical trial activities.



PRF's Mission:

To discover treatments and the cure for Progeria and its aging-related disorders.

Progeria is a fatal, "rapid aging" disease that afflicts children, who die of heart disease at an average age of 14 years – the same heart disease that affects millions of normal aging adults.

Because of Progeria's connection to general heart disease and aging, what we learn from Progeria research has the potential to benefit all of us.

Message from the President and Executive Director

Hello everyone,

At a **TedX event in Charlottesville*** in November, 2013, **Dr. Leslie Gordon**, PRF's Medical Director, shared her "Secret Sauce" for making anything possible. Dr. Gordon urged audience members to apply a version of this secret sauce to their own personal obstacles; her ingredients are a reflection of all that PRF has, and will, accomplish. I asked her to share those words with you in this issue:

Start with a refusal to believe in the concept of impossible. It may seem like more than you can handle, but it is not.

Understand your enemy (Progeria) as best you can while conquering it. Discovering the gene allowed researchers to understand how progerin worked and what drugs might defeat it, allowing a cure to seem within reach.

Seek the truth: Take the thousands of pieces of information and gain clarity from them to understand the disease better in our search for treatments and cure.

Each grain of sand is a part of the larger picture, and you never know what that picture is until you dive in and understand what's going on. With Progeria, it's the connection to aging – we are informing the aging field in ways no one ever thought of, and vice versa.

Remain laser focused on what matters most; the children. Thinking about them every day keeps us on track. And the most effective way to stay laser focused is collaboration; we are much better working together than we could ever be working alone.

Maintain a healthy dose of discontent: the successes (gene discovery, treatment) give us momentum and a way to push the work forward to where we must go, but it's never good enough until it's the cure.

Love is the most important ingredient. It threads through every one of the other ingredients. The children are inspiring, reaching into everybody's heart and minds so everyone will do their very best when working to to save children with Progeria.

All of you contribute to this recipe that drives PRF's quest for the cure. Thank you for helping to make that effort – and the tremendous strides we've made thus far – possible.

Together, we *WILL* find the cure!

Audrey Gordon

Audrey Gordon, Esq.
President and Executive Director

*To view the entire talk, go to *www.progeriaresearch.org/tedx*

In Loving Memory..!

Gone from our sight, but never our memories ~
Gone from our touch, but never our hearts.

Sam, *17 years old, from the US*

Teresa, *15 years old, from Italy*

We have lost a dear friend to the Progeria community in ***Bill Sample****, founder of the Sunshine Foundation and Progeria reunions.*

Study Finds Trial Medications Increase Lifespan for Children With Progeria

The best news yet...

In 2012 the first trial results showed us that the farnesyltransferase inhibitor (FTI) lonafarnib helped the children gain additional weight, improve bone structure and/or, most importantly, experience increased flexibility of blood vessels (*Gordon et. al., PNAS, October*). In 2013, we saw evidence that lonafarnib may decrease stroke, headache and seizure rates (Ullrich et al., Neurology). Now, in 2014, 6 years have passed since the children began taking the drug, and we are beginning to see what we had hoped for: that those improvements may translate into longer lifespan (*Gordon et al., Circulation*). The new study shows a statistical estimate of 80% reduction in risk of death for children on treatment, and an average estimated survival increase of 1.6 years within the 6 years of treatment. There were 21 deaths in untreated versus 5 deaths among treated children. **Time will tell if the estimated life extension is longer than 1.6 years.** Study researchers will re-evaluate survival extension several years from now, and ask whether that number can be increased after children are on the drug for a longer period of time.

The study notes that the two additional drugs added later as part of the PRF-funded "Triple Trial", pravastatin and zoledronate, may also contribute to this finding. However, because lonafarnib is the drug to which everyone was exposed, and it has shown cardiovascular benefit in Progeria, it likely plays the biggest role in increased lifespan.

July 2007: Sammy arrived from Italy to enroll in the 1st-ever Progeria clinical drug trial. Here he is pictured here taking the FTI lonafarnib for the first time.

March 2014: Zoey undergoes testing at her recent clinical trial visit to Boston Children's Hospital

Collaborating For Success... The study, published in the American Heart Association's premier journal *Circulation*,* was a collaborative effort between The Progeria Research Foundation, Brown University Center for Gerontology and Healthcare Research, Hasbro Children's Hospital, Boston University and Boston Children's Hospital. PRF's International Registry was essential to this study, as it tracks the Progeria population worldwide over time in a confidential manner.

*Impact of Farnesylation Inhibitors on Survival in Hutchinson-Gilford Progeria Syndrome, Leslie B. Gordon, MD, PhD, Joe Massaro, PhD, Ralph B. D'Agostino Sr., PhD, Susan E. Campbell, MA, Joan Brazier, MS, W. Ted Brown, MD, PhD, Monica E Kleinman, MD, Mark W. Kieran MD, PhD and the Progeria Clinical Trials Collaborative; *Circulation*, May 2, 2014 (on line).

A link to the full article and PRF's press release containing more details of study design and findings can be found at ***www.progeriaresearch.org***

"This is the first study to assess whether treatments influence patient survival, and thanks to a robust PRF registry and the clinical trials, we have been able to conclude that lifespan extension is possible for children with Progeria"

- Leslie Gordon, MD, PhD, lead author of the study, and Medical Director for PRF.

How Could This Help All of Us?

In a companion invited commentary on this study by aging experts Drs. Junko Oshima, Fuki Hisama, and George Martin at the University of Washington, authors address this very question: "Of major biomedical interest have been reports that small amounts of progerin can be detected in human tissues, including human arteries, and that these amounts increase with age. These observations now raise the important question of the extent to which progerin contributes to human atherogenesis (heart disease in the general population)." (*Oshima, Hisama and Martin, Circulation, 2014*)

Our History, Our Future...

In just 15 years, PRF has driven the research that discovered the gene, treatments and now life-extending treatment. Together, we will keep pushing forward in our quest to find the cure. **Thank you for making this remarkable progress possible!**

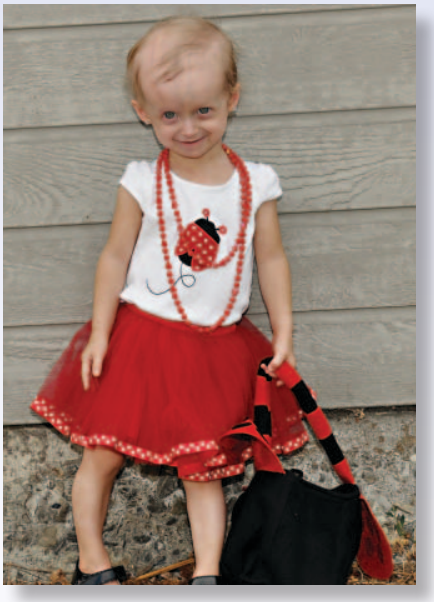
- 2003: Gene Discovery
- 2007: First Trial
- 2012: First Treatment
- 2014: Longer Life
- 20XX: CURE!

THANK YOU ALL for supporting the research that not only has brought us to this pivotal point, but also allows us to continue working to discover drugs that will extend life even further.

Clinical Trial Update

In our last issue, we announced that the "Triple Trial" would be extended and expanded so that every child can have access to treatment that could give them longer and healthier lives. This PRF-funded extension and expansion continues, as up to 41 new children from 24 countries speaking 15 languages join the 37 children currently enrolled.

Important Trial Expansion Details: During this last trial phase, all children will be taking lonafarnib alone while the trial team analyzes the many thousands of data elements (each child underwent over 100 tests per visit!)on the three-drug therapy phase of the trial. The triple therapy trial was pre-designed to include lonafarnib, pravastatin, and zoledronate. The hope is that adding two additional drugs to lonafarnib will boost the beneficial effects of the single drug therapy. While we know that lonafarnib is helping the children, it is still too early to tell if the other two are boosting the benefit. Usually, clinical trials run their course and the patients are taken off all the drugs until the data is analyzed to see if it helps; this could take years. PRF and the Boston Children's Hospital team have made the important decision to add two years of lonafarnib treatment for several crucial reasons. This extension and expansion allows additional time for the trial team to explore other potential benefits and track any long-term side effects of lonafarnib, including lifespan (see *Circulation* study described on page 4). Moreover, it allows us to continue exploring additional treatment options while giving all known children living with Progeria today the opportunity to participate in a clinical trial.

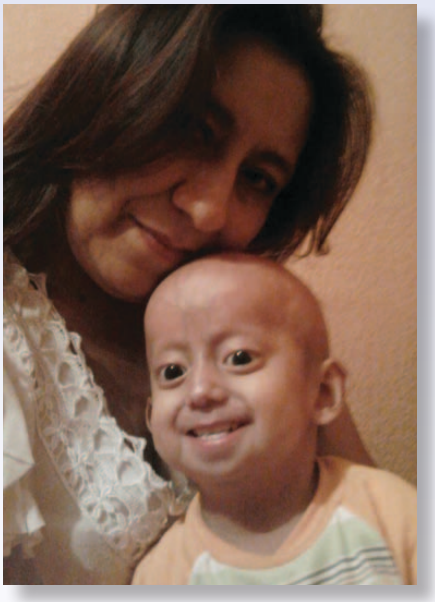


"All I could think was FINALLY, FINALLY it's here – medicine that will improve my daughter's life, help her to live longer and healthier. It was overwhelming and amazing."

– Heather, Carly's mom, during her first trial visit last summer.

"We are grateful and excited to start the clinical trial, and waiting for the day Yusi can meet more children like her."

– Mother of Yusally, 13 years old, from Brazil, who plans to come to Boston for the first time next month.



"We are very happy with the visit…To know that we will have a better quality of life for my baby makes me feel amazing, as my wife says he is a "Warrior of Life."

– Father of Angel, 3 years old, from Mexico, scheduled to arrive in Boston for his initial clinical trial visit in August.

We have raised $1.5 million of the $3 million* needed to fund this trial expansion so that every child has a chance to participate. THANK YOU for making this possible for Yusally, Angel, Carly and the other children. Let's keep going – we're half-way there!

* Great News! Due to a reduction in trial visits, we were able to reduce the costs from the original $4 million.

PRF Awards Seven More Research Grants

As of June 2014, PRF has provided over $5 million to fund 54 grants for Progeria-related research projects performed in 17 states and 10 other countries! We solicit proposals worldwide and through our scientific workshops, striving to fund research targeted at developing treatments and the cure for Progeria as rapidly as possible.

Brian Snyder, PhD, Associate Professor of Orthopedic Surgery, Harvard Medical School and Associate Director of The Center for Advanced Orthopedic Studies, Beth Israel Deaconess Medical Center, Boston, MA.

"Characterization of the Musculoskeletal, Craniofacial and Skin Phenotypes of the G608G Progeria Mouse"

Dr. Snyder along with post-doctoral candidate Ara Nazarian, PhD will analyze skeletal disease and changes with treatment in a Progeria mouse model using an advanced computed tomography (CT)- based structural rigidity analysis. Drs. Snyder Nazarian are a crucial part of the human clinical trial team in Boston. This analysis will mimic their human studies showing skeletal rigidity abnormalities in Progeria, which were improved with lonafarnib treatment. His team will also conduct biomechanical studies to characterize changes in shape of the bone, calcification of the blood vessels, changes in the skull and the skin, and assess the extent to which these changes are inter-related and whether these changes can be used to track disease severity and response to new potential treatments for Progeria.

Katherine Wilson, PhD, Professor of Cell Biology, Johns Hopkins School of Medicine, Baltimore, MD

"Natural expression of progerin and consequences of reduced lamin A tail O GlcNAcylation"

Dr. Wilson's lab studies the 'trio' of proteins (lamins, LEM-domain proteins and BAF) that form nuclear 'lamina' structure, to understand how mutations in these proteins cause HGPS (progeria) and other lamin-associated diseases. Progerin has been viewed as an 'unnatural' form of lamin A. However new work suggests progerin is expressed at high levels at two specific times and places in the human body—after birth when the newborn heart is being remodeled (closure of the ductus arteriosus), and in cells (fibroblasts) exposed to ultraviolet (UV-A) light. This suggests progerin is a natural gene product that is expressed at specific times, for specific unknown reasons. A basic understanding of these proposed 'natural' roles of progerin may identify new pathways that could be targeted therapeutically in HGPS.

Dr. Robert Goldman, PhD, Stephen Walter Ranson Professor and Chairman of the Department of Cell and Molecular Biology at Northwestern University Feinberg School of Medicine, Chicago, IL

"New Insights into the Role of Progerin in Cellular Pathology"

Dr. Goldman's project aims to 1) thoroughly characterize the nature and function of the protein modifications that occur on the 50 amino acid fragment of lamin A that is missing from its mutant form progerin in HGPS and 2) address how the progerin mutation affects the localization and behavior of lamin A during the cell cycle. This study may provide important new insights into how progerin affects nuclear function, and facilitate new therapeutic interventions for HGPS patients by targeting key disease modifications to lamin A.

Brian Kennedy, PhD, President and Chief Executive Officer, Buck Institute for Research on Aging, Novato, CA

"Small Molecule Aging Intervention in Progeria"

Dr. Kennedy leads a team of 20 principal investigators in their research in the basic biology of aging and discoveries into new ways of detecting, preventing and treating age-related conditions including heart disease. Mutations in A-type nuclear lamins give rise to a range of diseases termed laminopathies, which are associated with cardiovascular disease, muscular dystrophy and Progeria. Among these are a subset, which give rise to progeroid syndromes that resemble accelerated aging. The question as to whether or not progerias are mechanistically related to the events that drive normal aging has plagued the aging field for decades. Small molecules have recently been identified that slow aging (rapamycin) and protect against age-associated chronic diseases (rapamycin and resveratrol). If Progeria is linked mechanistically to normal aging, these small molecules and others that are emerging may be effective agents in its treatment. In this study, Dr. Kennedy's lab will employ mouse models of Progeria to evaluate the efficacy of resveratrol and rapamycin (as well as derivatives of both agents) toward ameliorating disease pathology.

Christopher Carroll, PhD,
Assistant Professor, Department of Cell Biology, Yale University, New Haven, CT.

"Regulation of progerin abundance by the inner nuclear membrane protein Man1"

The molecular mechanisms that control the abundance of Lamin A protein are not well understood. Dr. Carroll's lab has previously shown that the inner nuclear membrane protein Man1 prevents the accumulation of Lamin A in human cells. This study will determine whether Man1 also acts to limit the accumulation of progerin, the mutant form of Lamin A that causes Progeria, and if so, whether this pathway represents a novel target for therapeutics that delay or prevent the accumulation of progerin in children with HGPS.

Katharine Ullman, PhD,
Adjunct Professor, Biochemistry Research and Professor, Oncological Sciences, University of Utah, Salt Lake City, UT

"Elucidating how progerin impacts the role of Nup153 in the DNA damage response"

This project aims to gain new insight into the etiology of Progeria by tackling how mutation in lamin A – which results in expression of a mutated form of lamin A termed progerin – alters the function of the protein Nup153, especially in the context of DNA damage. Nup153 is a component of a large structure called the nuclear pore complex and is recently recognized to participate in the cellular response to DNA damage. Lamin A is known to interact with Nup153 and also participates in the response to DNA damage. Dr. Ullman will study this functional intersection, and build on these connections with the goal of rapidly integrating new information into the context of HGPS.

Dr. Gerardo Ferbeyre, PhD, Professor, Department of Biochemistry, University of Montreal, Quebec, Canada

"Control of progerin clearance by defarnesylation and phosphorylation at serine 22"

The accumulation of progerin causes Hutchinson-Gilford Progeria Syndrome. The ideal treatment for HGPS should prevent the accumulation of progerin by decreasing its synthesis or promoting its degradation. However, little is known about the normal turnover of lamin A or progerin. The accumulation of progerin in the nuclear wall is controlled by farnesylation, and phosphorylation (adding a phosphate group to lamin A at a specific site on the protein). Dr. Ferbeyre's group will identify enzymes regulating the addition of phosphate to lamin and enzymes mediating protein breakdown that mediate lamin A turnover. This information may help to identify drugs that stimulate progerin turnover and improve HGPS patients.

For more details on the application process and the grants PRF has funded, please visit *http://www.progeriaresearch.org/research_funding_opportunities/*

Workshop organizer and co-author of the Cell *article Tom Misteli moderates the session "The Next Phase for Treating Progeria."*

HAND IN HAND
Basic & Clinical Science Working Together Toward the Cure

The PROGERIA RESEARCH FOUNDATION
SCIENTIFIC WORKSHOP
April 24 - 26, 2013
Bethesda North Marriott Conference Center
Bethesda, MD, USA

Prestigious Journal Affirms Importance of 2013 PRF International Workshop

Article cites conference as indicator of rapid progress

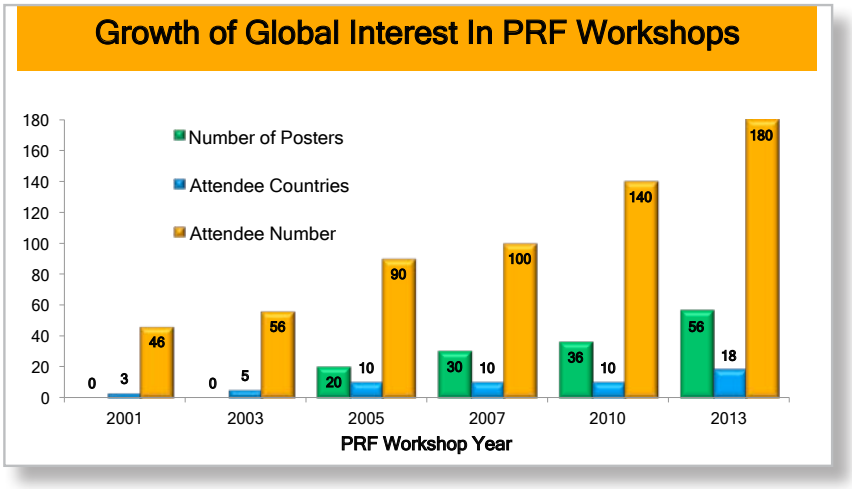
Progeria – A paradigm for translational medicine, Gordon, LB, Rothman, FG, Lopez-Otin, C, Misteli, T, *Cell*, Volume 156, Issue 3, 400-407, 30 January 2014 was written by PRF workshop organizers and appears in *Cell*, one of the highest impact journals in the world. The article details the latest basic science by researchers from 18 countries who gathered in Washington, DC for a 3-day conference at the **7th Progeria Research Foundation International Workshop**, "Hand in Hand: Basic & Clinical Science Working Together Toward the Cure."

The article states: *Progress in the HGPS field has been remarkably rapid over the last decade, and if the most recent Progeria Research Foundation Workshop is any indication, there is no sign of slowdown… Looking back over the past 10 years in the progeria field, we see a roadmap for how to optimize our chances of tackling a disease once its molecular basis is uncovered… We have learned many important lessons from a very rare disease, and they will undoubtedly be applicable to many other diseases…."*

The growth and rapid progress continues, more planned to get us to the cure!

PRF's programs are thriving and expand annually with increasing numbers of children identified, researchers involved, and awareness raised. All of PRF's activities work cohesively to provide the core structure essential not only to drive the field of Progeria forward, but also to discover what Progeria can tell us about heart disease and aging.

From 2012 to 2013, our program growth continued at an impressive pace. This includes a 12% increase in the number of known children, 29% increase in scientific workshop participation, and 50% increase in public awareness – wow!



For more details on PRF's programs and services, check out PRF By The Numbers at progeriaresearch.org/prf-by-the-numbers

10 Core PRF Activities That Support Our Mission

2013 ACTIVITY	PRF PROGRAM	CUMULATIVE ACTIVITY
12 children from 5 countries	International Patient Registry	193 children from 48 countries and all continents
7 children diagnosed from Bulgaria, India, Mexico & Tanzania	Diagnostic Testing Program	111 children diagnosed
4 cell lines from donors; cells sent to 9 teams in 5 countries	Cell & Tissue Bank	194 samples from 185 donors; cells sent to 60 teams in 14 countries
5 children enrolled; 15 treatment guidelines sent to 5 countries	Medical & Research Database	126 enrolled; 455 treatment guidelines sent to 36 countries
Funded Triple Treatment Trial Expansionl	Clinical Trial Funding & Co-coordination	3 clinical trials funded since 2007
9 grants awarded	Basic Research Grant Funding	54 grants to 34 labs in 11 countries; funding total >$5 million
"Hand in Hand: Basic & Clinical Science Working Together Toward a Cure", Washington, DC	International Scientific Meetings	11 meetings: 7 general workshops and 4 sub-specialties
65 events (25 annual) & over 400 new volunteers	Volunteer Program	Nearly 4,000 volunteers worldwide have helped raise awareness and funds
1 language added: Swahili	Translations Program	26 languages
12 new children identified and 650 million people reached through media	Public Awareness & Find The Other 150 Campaign	112 children from 39 countries; over 1.65 billion people exposed to Progeria and PRF's work

2013 Highlights:

The premiere of Life According to Sam (LATS) made 2013 a transforming year for PRF in terms of public awareness and fundraising. PRF's social media followers increased by 50% and revenue increased by 51%, with the majority of the additional funds coming from the Kraft Challenge and LATS viewers. Nearly 1.2 million people saw this story of love, life and hope for children with Progeria, raising awareness of the disease and PRF's quest for the cure in a unique and uplifting way.

The expansion of the Triple Trial began in July 2013, with the first of up to 40 new children arriving at Boston Children's Hospital. Initial enrollment for the Triple Trial ended in 2010, and since then many children with Progeria have been identified. The expansion allows children found after initial enrollment ended to participate. With the historic discovery that one of the drugs being tested (lonafarnib) improves some disease features, including the cardiovascular system, PRF is making it possible for every child to have access to the only current treatment for Progeria, while we continue to search for even more effective treatments and ultimately the cure.

Nine new research grants were awarded in 2013, contributing to 14 active projects – an all-time high for both figures. As of 12/31/13, PRF is proud of a funding rate of 50.5%. Our grantees are leading the charge for Progeria's future scientific discovery, changing the landscape of Progeria research and giving the world ever-increasing hope for treatments and cure.

The exponential increase in published Progeria studies that both advance the field and demonstrate Progeria's connection to aging continues. In 2013 alone, the number of peer-reviewed scientific publications was an astounding 93. PRF's critical impact on Progeria-related research is evident. In 52 years, from 1950-2002, the average number of peer reviewed publications on Progeria was less than two per year. From 2003-2013, 458 articles were published, representing a remarkable average annual increase of over 2,000% since 2003, the year PRF co-discovered the Progeria gene – remarkable!

New partners, New hope: Thanks mainly to *Life According To Sam* and the Kraft Challenge, dozens of stories and thousands of social media posts introduced Progeria and The Progeria Research Foundation to people that otherwise would never have known about us. The number of donations increased by 31%, with over 3,600 new supporters – many coming from the sports, entertainment and corporate sector – to help fund the trial expansion. While we have much work to do to get to the cure, this remarkable momentum will help us to accomplish our mission.

Many thanks to all of you for making such tremendous advancements possible. With your steadfast support, we will work to ensure that 2014 and beyond brings us ever-closer to curing children with Progeria. Together, we *WILL* find the cure!

The Boston Globe

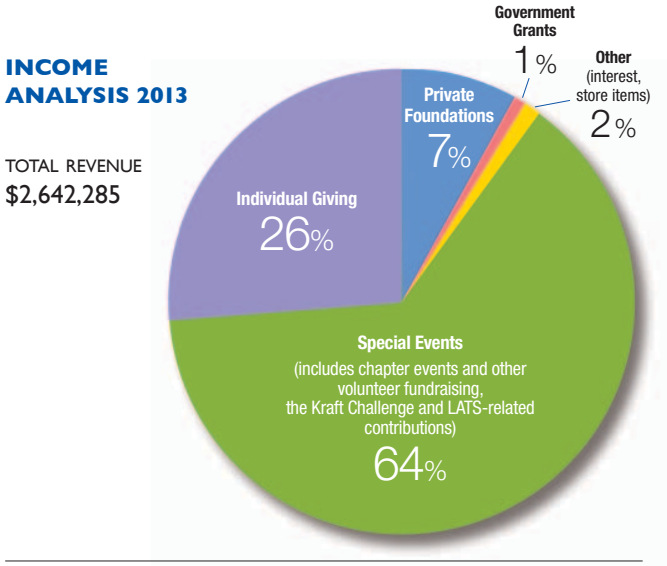
THURSDAY, DECEMBER 26, 2013

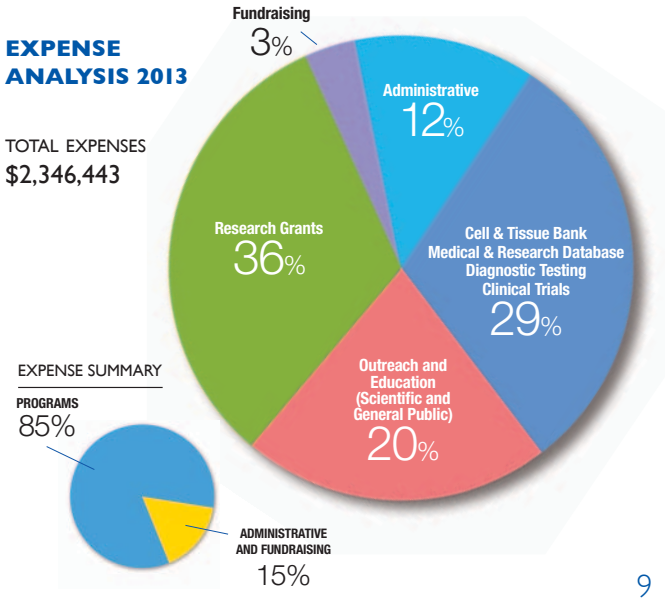
A rare life gathers teams of supporters

Youth's aging disease spurs research, film

By James Sullivan

The December 2013, front-page Boston Globe article highlights the success of the Kraft challenge and HBO's premiere of Life According to Sam.





Life According to Sam a Huge International Hit

HBO Documentary wins numerous awards, heightens awareness worldwide

Last year, starting with its premiere in January 2013 at the prestigious Sundance Film Festival, *Life According to Sam (LATS)* captivated audiences and won ten festival awards, including the Audience Award and Best Feature Documentary. More recently, this 90-minute film about Progeria, the extraordinary Sam Berns, his parents' and PRF's search for a cure, and the family's ability to live life to its fullest, won two prestigious awards: a Christopher Award, presented to filmmakers whose work "affirms the highest values of the human spirit," and a Peabody Award, given to "stories that matter." Indeed, its story of love, life and hope for children with Progeria continues to "matter" to more people every day, which translates into more awareness of this rare disease and the importance of PRF's mission to find the cure.

Accepting the Peabody Award, Directors Sean Fine and Andrea Nix Fine thank Sam, Leslie Gordon (far left) and Scott Berns (2nd from the left) for allowing them to enter their lives and "make us better storytellers."

Sam and Dave Matthews recorded a public service announcement for the DVD. You can also see it on PRF's YouTube channel, www.youtube.com/user/progeria123

Share this inspiring film with your family and friends! LATS is now available ON DEMAND and by purchasing the DVD from HBO at ***http://store.hbo.com/****. The DVD also includes Sam's TedX talk and a heartwarming message from Sam and his friend Dave Matthews.*

Attention Teachers and Students: Bring LATS to Your School!

Life According to Sam is also a powerful tool for engaging middle and high school students in learning. The film sheds light on the biology of disease, creative problem solving in the face of adversity, and lessons in peer inclusion. PRF has created a discussion guide for teachers, to help generate dialogue about the important issues the film explores. Contact ***info@progeriaresearch.org*** *for more details.*

New England Patriots owner Robert Kraft attends the October 2013 HBO premiere of LATS in New York City. After meeting Sam at a team practice and seeing the film, Mr. Kraft was inspired to donate a $500,000 matching gift to help fund the trial expansion. "This is a must-see film", he says. "It will make you laugh. It will make you cry. And, most importantly, I think it will motivate people to want to do more to help."

Photo Credit: Thos Robinson/Getty/HBO

Sam and Katie Couric on the set of her show the day after the HBO premiere. Sam spoke about overcoming obstacles, and Leslie and Scott discussed the progress toward a cure for Progeria. Katie and her crew said it was one of the most meaningful and popular interviews they ever conducted. Watch it on KatieCouric.com

"*Watching an unbelievable documentary called* ***Life According to Sam.*** *Inspiring in every way."*

-- @JamesWolk, PRF (@progeria) and #lifeaccordingtosam Twitter follower

Sam G. Berns
10/23/96 - 01/10/14

Sam was diagnosed with Progeria at 22 months of age. Driven by Sam's diagnosis and the enormous lack of medical information and research-related resources dedicated to Progeria, Sam's parents, Drs. Leslie Gordon and Scott Berns, together with Audrey Gordon, their family, friends and colleagues, created The Progeria Research Foundation to drive the research that will ultimately lead to a cure.

The entire PRF community mourns the loss of this remarkable young man who was not only the motivation for PRF's creation, but also an extraordinary scholar, thinker, musician and friend who touched millions of people worldwide.

With the 2013 broadcast of Life According to Sam, his courage and spirit moved viewers deeply. Sam also shared his life philosophy in his wildly popular TEDx talk last October. In the months following his passing, we have seen thousands of emails, tributes, Facebook posts and tweets about Sam even though most had never met him but felt they knew him through the film and his TedX presentation. One word appears in nearly all of these messages: **inspiration**. How wonderful to leave such a legacy!

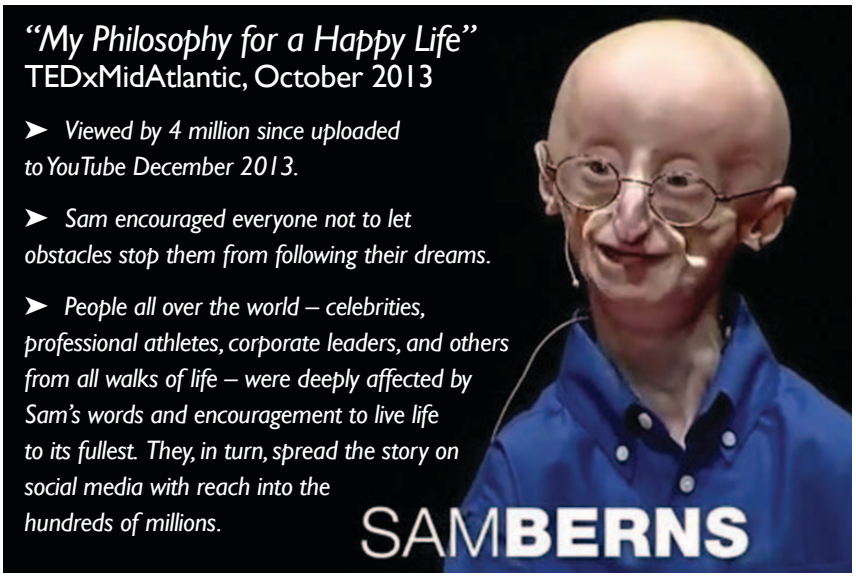
One major belief Sam had was the concept of teamwork. He felt strongly that it takes an entire team working together to be successful. That's how PRF has gone from obscurity to treatment - working with partners like you – and that's how we will get to the cure.

We will celebrate Sam's life by moving ahead with resolve. As Sam now famously says, "Being brave isn't supposed to be easy – but for me, it's the key way to keep moving forward." We agree. So forward it is.

We will finish what we started. Together, we *WILL* find the cure.

"My Philosophy for a Happy Life"
TEDxMidAtlantic, October 2013

- *Viewed by 4 million since uploaded to YouTube December 2013.*
- *Sam encouraged everyone not to let obstacles stop them from following their dreams.*
- *People all over the world – celebrities, professional athletes, corporate leaders, and others from all walks of life – were deeply affected by Sam's words and encouragement to live life to its fullest. They, in turn, spread the story on social media with reach into the hundreds of millions.*



To see the full talk, go to *www.progeriaresearch.org/tedx*

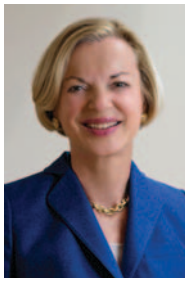
PRF *ON THE MOVE!*

PRF Welcomes 3 New Board Members

Our leadership team is growing…

Roger Berkowitz is President and CEO of Legal Sea Foods. He also serves on the board of directors for the Federal Reserve Bank of Boston and the Regional Selection Panel for the President's Commission on White House Fellowships. He is a member of the MA Workforce Training Fund Advisory Committee and a member and past President of the MA Restaurant Association. Roger also serves on many non-profit boards including Dana-Farber Cancer Institute, Children's Hospital Boston (Advisory Board), UNICEF, and the Boston Children's Museum. He is a member of the Board of Overseers, Brandeis International Business School, is a Trustee of both Suffolk University and Salem State University, and serves on the leadership council at the Harvard School of Public Health.

Larry Mills is the Executive Vice President of the Holt Companies, based in San Antonio, Texas. After holding various positions with the companies in the areas of parts operations, marketing, sales and human resources, his areas of focus now include strategic planning, marketing, leadership development, and organizational development. He is the founder of Holt Development Services, Inc., which is based on the Values Based Leadership approach to business. Larry serves on the board of directors of the San Antonio Spurs, Clarity Child Guidance Center and Children's Hospital of San Antonio Foundation. He is a member of the Society of Human Resource Management, the American Society of Training and Development, and the Ethics Officers Association.



Joining our Board of Advisors is **Elizabeth N. Nabel**, MD, President of Brigham and Women's Hospital in Boston, MA, Professor of Medicine at Harvard Medical School, and former Director of the National Heart, Lung, and Blood Institute. A cardiologist and distinguished biomedical researcher, her honors include the Amgen-Scientific Achievement Award; two Distinguished Achievement Awards and the Eugene Braunwald Academic Mentorship Award from the American Heart Association; the Lewis Katz Research Prize in Cardiovascular Research from Columbia University; and six honorary doctorates. Her colleagues have elected her to the American Academy of the Arts and Sciences, the Institute of Medicine, the Association of American Physicians, and the American Society of Clinical Investigation. She is a Fellow of the American Association for the Advancement of Science, is on the editorial board for the New England Journal of Medicine and Science Translational Medicine, and is editor of Scientific American Medicine.

We are honored to have these renowned leaders in the fields of business and medicine join in directing PRF's mission.

PRF Receives Research!America Award for Advancing Research

PRF received Research!America's prestigious Paul G. Rogers Distinguished Organization Advocacy Award at a ceremony in Washington, DC, where leaders from government, industry, academia and nonprofit organizations gathered to honor those who have made a significant impact in advancing research. Recognized for bringing Progeria from obscurity to successful translational research, Mary Woolley, president and CEO of Research!America said, "The Progeria Research Foundation is a trailblazer in the research advocacy community. Their passion and dedication to improving the lives of patients and families is a model for others."

PRF Board Chair Dr. Scott Berns, Mr. Rogers' daughter Laing Rogers Sisto, wife Becky Rogers, PRF Medical Director Dr. Leslie Gordon, award presenter Dr. Betsy Nabel, and PRF Executive Director Audrey Gordon

PRF Achieves Highest 4-Star Rating

PRF has also been awarded four (out of four!) stars from Charity Navigator, America's premier independent nonprofit evaluator. Their in-depth, objective analysis identified PRF's strong financial and organizational status: "PRF adheres to good governance and other best practices," the review panel noted, "and consistently executes its mission in a fiscally responsible way."

We are thrilled that PRF is being recognized in such significant ways for its important and accomplished work for children with Progeria. Kudos to all of YOU, who make such achievements possible with your unwavering support.

Social Media Madness!

In just the last six months, PRF's direct reach through our social media channels has soared from 50,000 to nearly 500,000 – that's not a typo! Our followers hail from 45 countries speaking 35 languages. And thanks to all of you that share posts and retweet our messages, the reach extends to millions more around the globe. Such vast exposure of Progeria and PRF's work is helping to find more children to help, and more supporters to help us get to the cure.

Keep spreading the word – it's working!

Boston Bruins Hold Progeria Awareness Night

In November, a sold-out crowd of hockey fans cheered not only for their favorite team, but also for PRF. Starting with Sam's honorary captain status and dropping the puck (for which

Team Captain Zdeno Chara and Sam on the ice for the ceremonial puck drop

he received a standing ovation!), details about Progeria, PRF's mission and how people can help were announced and shown on the jumbotron throughout the evening. Half the proceeds from the 50/50 raffle – which raised a record-high $18,000! - were also donated to PRF. Many thanks to our friends at the Boston Bruins Foundation for this tremendous opportunity to raise awareness and funds for Progeria research.

It's a Wrap!

Our 2014 Night of Wonder Gala, Lights, Camera, CURE! was one for the record books. A sold-out crowd of 470 dressed to the nines to attend the much-anticipated event. Longtime supporters mingled with many new faces, all celebrating the honorees, PRF's successes, and the memory of Sam Berns.

From the eye-catching ice sculpture, to the candy-filled concession stand, to the white plumed centerpieces, guests were surrounded by the look and feel of old time Hollywood. The prestigious awards and moving speeches added to the wonder and excitement of the evening.

Together we raised a record breaking $500,000 for the programs and research that will bring us the CURE!

Gala Chair Debbie Mendelson Ponn welcomes the crowd

Guests were entertained by The Boston College Acoustics

Dr. Mark Kieran receiving the Science and Medicine (SAM) Award

Sheila Nevins, President of HBO Documentaries, gives a touching speech about her involvement with PRF and Life According to Sam

Many thanks to our lead sponsors:

Alice & Lew Berns
Leslie Gordon & Scott Berns
Bob & Gretchen Morrison
Debbie Mendelson Ponn
Boston Bruins Foundation
Sandra Bresnick & Peter Armenio
HBO
Hologic
Linda & Bob Mendelson
L & L Motors

Chapter and Volunteer Fundraising Events

So Vital to PRF's Mission!

"Inspirational" - that's the word that immediately comes to mind when we think of our dedicated chapters and all the other volunteers who work tirelessly to help children with Progeria. This ever-growing group now contributes close to 50% of our operating budget. How do they do it?! By organizing fun, mission-focused events that bring people together to share in the common goal of raising awareness and money for Progeria research. We simply could not fund the research or clinical trials that will get us to the cure without them.

THANK YOU ALL!

In the past year, our 8 chapters and other volunteers have held over 200 events - WOW! Here are photos from a few of them. See lots more on our Facebook page at www.facebook.com/ProgeriaResearch

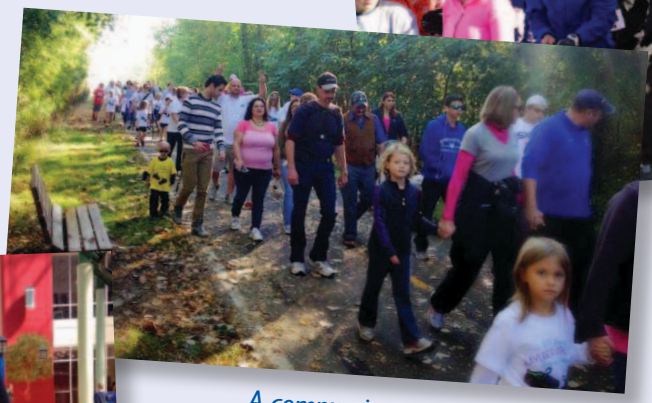
Many events are held each year. If you live nearby, we hope you'll participate in the next one!

Sammy & Niccolo have fun during **Hats ON for Progeria** day - Worldwide

Zach tees up at the 3rd **Zach Attack Golf Scramble**, Lexington, KY

Bob and Cam relax after the 5th Annual **Cam's Course Golf Scramble**, Butler, PA

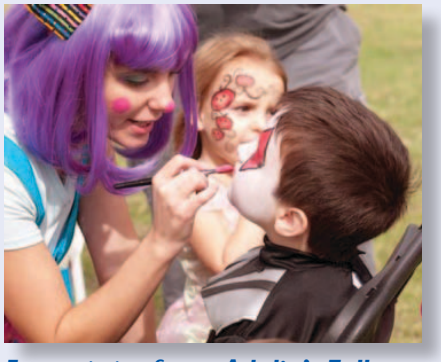
Cheering the start of the 3rd Annual **Turkey Trot**, Verona, NJ



A community comes together for the 8th Annual **Kaylee's Course**, Monclova, OH

Lindsay and a special supporter at the 8th Annual **Miles for Miracles**, Flat Rock, MI

Smiles from the many **Carly's Party** volunteers, Maumee, OH



*Face painting fun at **Adalia's Fall Festival,** Round Rock, TX*

*Dancing poolside last summer at **Make A Splash**, Flourtown, PA.*

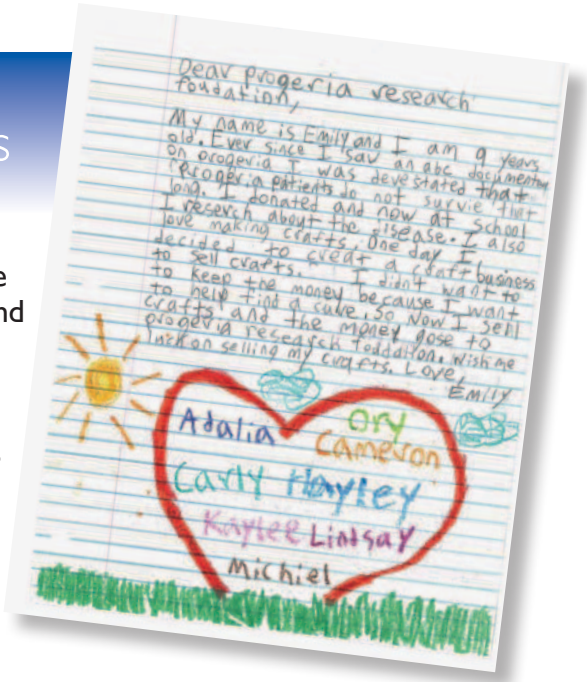
*Kevin, Chip & Zach check out the cars at the 8th Annual **Foose Braselton Bash**, GA*

We hope you're inspired to hold your own event, and if so we're here to help. Email volunteers@progeriaresearch.org and we'll get you started!

Spotlight on our Young Miracle Makers

"Kids Helping Kids" is an uplifting phrase we get to say quite often here at PRF. From organizing bake sales and walks, to spreading the word about Progeria through school reports and presentations, our youth volunteers are a remarkable group. Enjoy reading some of their stories.

Emily sent us this letter along with the money she raised from selling her homemade crafts. So sweet!



Mazzi, Rachel and Jesse

Penny Wars - What a great idea! Rachel and her friends collected 93,685 pennies for PRF at their middle school in Andover, MA. After 3 hours at the bank's change machine, they had some fun with the bills and were thrilled with the event's success – their smiles say it all!

Owen and the "Friends of Sam" in Foxboro, MA held a huge bake sale at John J. Ahern Middle School in Foxboro, MA. The event raised over $5,000, and is one of many local events the community has held in honor of Sam Berns.

Corey, Brady, Owen and Sam

Katherine P. (first on left, in blue dress) asked her fellow actors to support PRF by donating proceeds from their performance of Into the Woods, at the Grace Chapel, Lexington, MA. Now that's an award-winning performance!

Inspired by her affection for the Falcone boys, Julia has been organizing events for PRF for the past 2 years, including a dance and Walk for a Cure at Penn Charter High School. She also made and sold hair accessories, collected donations in lieu of gifts for her Sweet 16 celebration, and recently gave a TEDX talk at her school – whew!

Julia with Nathan and Bennett

Come join our team of Miracle Makers! Check out *progeriaresearch.org/get_involved/* for ideas and more information on how you can help find a cure.

Progeria Research Foundation
P.O. Box 3453
Peabody, MA 01961-3453

RETURN SERVICE REQUESTED

To learn more about how you can help, contact us:
info@progeriaresearch.org or call 978-535-2594

Adalia hopes you have a great summer!

goodsearch: an easy way to make a difference

Yahoo!-powered goodsearch© is a simple way to make a difference – just go to goodsearch.com and sign up to support The Progeria Research Foundation. Then each time you search the web, shop online (at the 3,000+ partner stores on goodshop© including top retailers like Amazon, Expedia and Staples), or dine out (at 10,000 gooddining© restaurants), PRF receives a donation. You also have access to 25,000+ discounts and coupons so you can save money and give back at the same time.

Your pennies per search can quickly add up, and there is no cap on how much money PRF can receive, so start searching and shopping today!

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