



Global Study Published in *JAMA* Finds Treatment with Lonafarnib Extends Survival in Children with Progeria

First-Ever Therapy to Demonstrate Survival Benefit in Progeria

With No Approved Treatment Options, Children with Ultra-Rare, Fatal, Rapid-Aging Disease Die of Heart Disease at an Average Age of 14 Years

PEABODY, MA, April 24, 2018 — A new study published in *The Journal of the American Medical Association* (JAMA) reports that lonafarnib, a farnesyltransferase inhibitor (FTI), helped extend survival in children with Hutchinson-Gilford Progeria Syndrome (HGPS), or Progeria, an ultra-rare and fatal disease that causes premature aging in children. Children with Progeria live an average 14 ½ years, dying from heart disease typically associated with old age. Authors from Boston Children's Hospital and Brown University tracked more than 250 children from six continents to demonstrate a link between lonafarnib treatment and extended survival.

Progeria is caused by a genetic mutation that results in an overabundance of the protein named progerin. Accumulation of progerin within a cell is typically seen in normal aging, but the rate of accumulation is highly accelerated in Progeria, causing progressive cellular damage and resulting in atherosclerotic heart disease.

Lonafarnib, originally developed by Merck as a potential cancer therapeutic, inhibits farnesyltransferase, an enzyme that facilitates progerin production. The FTI prevents the mutant protein from incorporating into the cellular wall where it causes much of its damage.

In the clinical trial, 27 children with Progeria received oral lonafarnib (150 mg/m²) twice daily as a monotherapy. The control arm of this study consisted of children with Progeria with similar age, sex and continent of residency as the treated patients, who were not part of the clinical trial and therefore did not receive lonafarnib. The results demonstrated that treatment with lonafarnib alone compared with no treatment was associated with a significantly lower mortality rate (3.7% vs. 33.3%) after a median of 2.2 years of follow up.

The study was funded by the non-profit organization, The Progeria Research Foundation (PRF).

"My lab did some of the original research on cellular and mouse models that showed potential benefit of this class of drugs for Progeria," said National Institutes of Health Director Francis S. Collins, MD, PhD. "It was encouraging to see those results translated into a clinical trial. Yet demonstrating effectiveness of

treatments in this small population of children with this rare fatal disease is a major challenge. Thus, I'm particularly encouraged by these latest findings," said Dr. Collins.

"This study published in *JAMA* shows evidence that we can begin to put the brakes on the rapid aging process for children with Progeria," said Leslie Gordon, MD, PhD, co-founder and Medical Director for PRF, and lead study author. "These results provide new promise and optimism to the Progeria community," said Dr. Gordon.

To date, PRF has funded four clinical trials and hundreds of scientific studies aimed at discovering new treatments and the cure for children with Progeria. Previous studies sponsored by PRF linked lonafarnib to improvements in clinical trial endpoints associated with atherosclerosis and stroke, two hallmarks of Progeria.

Progeria occurs in one in 20 million people, with nearly 110 children identified through the PRF International Progeria Registry (<https://www.progeriaresearch.org/international-progeria-registry/>) and an estimated more than 250 undiagnosed children worldwide. PRF seeks to find and help all children with Progeria.

"At PRF, we are working tirelessly to fund new scientific breakthroughs for children living with Progeria. This study shows us that the clinical trials conducted today are our best hope for saving for these children in the future," said Meryl Fink, President and Executive Director, PRF. "Based on the promising results from this study with lonafarnib, we feel a stronger sense of urgency than ever. Today's milestone marks a new beginning for these children and their families. Every day and every moment count. PRF's goal is to find the cure for Progeria and this study brings us one more step towards that goal," said Fink.

About The Progeria Research Foundation

The Progeria Research Foundation (PRF) was founded in 1999 by the family of Sam Berns in response to the complete lack of attention to, and progress being made in, Progeria research. The original mission: to discover the cause, treatments and cure for Progeria. In 2003 the PRF Genetics Consortium discovered the Progeria gene, a collaboration led by Dr. Francis Collins, then as the Director of the National Human Genome Research Institute, and who is currently Director of the National Institutes of Health (NIH). Today, PRF continues to be the only organization in the world solely dedicated to finding treatments and the cure for Progeria and its aging-related conditions, including heart disease. The organization fills a void, taking these children out of the background where they had been for more than 100 years and putting them and Progeria at the forefront of scientific efforts. For more information and to donate to PRF, please visit www.progeriaresearch.org.

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