

Project Summary for The Associazione Italiana Progeria Sammy Basso July 3, 2019

➤ **Final Stages of the Phase 2 Trial of Everolimus Combined with Lonafarnib**

With nearly half the children and young adults having completed their trial visits, we are excited to be in the final stretch of patient visits for the Progeria 2-drug clinical trial that A.I.Pro.S.B. generously supported when Phase 2 began in July 2017.

Recap of Trial Background

The objective of this Phase 2 clinical trial is to determine whether or not the addition of a certain drug (everolimus) to the treatment (lonafarnib) is more beneficial for children with Progeria. While we are thrilled with the discovery that lonafarnib improves some aspects of Progeria, the children need additional treatments to thwart the fatal heart disease that develops. PRF and its research partners have discovered that while lonafarnib may block the toxic, disease-causing progerin from developing in the first place, everolimus appears to eliminate the progerin that does develop and attack the cells. Thus, the combination may prove to be a “one-two punch” to Progeria.

Trial Update

The trial is proceeding smoothly, and as per the established protocol. There are 60 participants (three withdrew, and an enrollment end date had to be set). Sixty is, statistically, the number of patients needed to determine effectiveness of the 2-drug combination. It is important to note that other children found after enrollment ended, or those who could otherwise not enroll before the cutoff date, are still able to take the treatment lonafarnib; PRF and the trial team secured approval for a separate, lonafarnib-only clinical trial for that purpose.

All participants have completed their first of two visits to Boston, and 24 have completed their end-of-study visits. There are 16 more scheduled in 2019, and the final 20 will finish in late 2020. After visit completion, a rigorous review of thousands of data points will take place, to determine if there has been a statistically significant change in certain aspects of Progeria. The results will then be submitted to a peer-reviewed scientific publication and published. The trial itself will be considered a success if certain pre-selected parameters are achieved by the children, deeming the combination of lonafarnib and everolimus a more effective treatment than lonafarnib alone.



8-year-old Prachi from India was in Boston for her final trial visit in May. She took a break from testing to play the piano at a local children's playhouse.



Trial objectives reached to date include full enrollment, successful arrangement of lodging and travel including procurement of required visas and passports (a growing challenge that is more difficult and restrictive each year), and budget decrease. Please see revised budget below, which details a decrease of approximately \$1,000,000. The main reasons include reduction from 80 to 60 participants, a Boston Children's Hospital grant that covers some expenses, and personnel changes. ***Your 2017, \$70,000 grant funded food, lodging and testing for both visits for 14 children!***

We are requesting a \$70,000 grant this year, to fund nearly all food, lodging, testing and interpreters for the rest of the children (16) coming to Boston (for their final visits) this year. The breakdown is as follows:

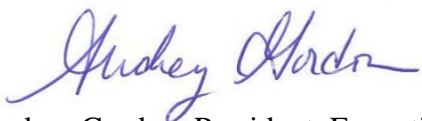
Testing for visit #2:	$\$2,672 \times 16 = \$42,752$
Food for visit #2:	$\$350 \times 16 = \$5,600$
Lodging for visit #2:	$\$210 \times 16 = \$3,360$
Interpreters (for 15 of the 16):	$\$1,400 \times 15 = \$21,000$
Miscellaneous additional expenses:	$\$2,288$

TOTAL: \$75,000 US

Progeria clinical trials offer the best chance to accomplish our mission, representing the culmination of years of research designed to discover ways to improve the health and lifespan of children with Progeria. The trials have also provided a plethora of information on the disease process. This information has been tremendously helpful to researchers as they work to discover new drug candidates and other findings that can advance the field of Progeria and aging-related conditions including heart disease, as well as help the children today.

We look forward to continuing our partnership, and cannot thank you enough for all your support.

Respectfully submitted,



Audrey Gordon, President, Executive Director



Michiel and his sister Amber will travel from Belgium to Boston for their final trial visit in August.

Budget for the Progeria Clinical Trial of Everolimus with Lonafarnib: An open-label, phase II Trial of everolimus with lonafarnib for 60 patients with Hutchinson-Gilford Progeria Syndrome and progeroid laminopathies.

Projection for entire trial: \$2,591,209

Funds spent to date (July 1, 2017 through June 30, 2019): \$1,595,975

Major Expense Categories:

Testing at Boston Children's Hospital (BCH) and Brigham & Women's Hospital: \$179,055
Consists of Lab tests (Blood work, etc.), Cardiovascular, Radiology, etc.

At-home blood tests: Estimated @ \$150/test: \$8,250

Travel: \$313,912

Airfare, visa, passport, taxi for child and one parent. Flights and visa/passport expenses = \$2,300 average per international traveler; flights = \$535 average per US traveler. A 10% increase per year is factored in.

Food per diem: \$30,770
\$30/day adult, \$20/day child

Lodging: \$37,403

\$30 per night at patient housing, for 7 nights. Figure factors in a few families having to stay at area hotels when patient housing is not available.

Staff: \$1,770,893

Trial Principal Investigators, Hospital and PRF Coordinators, Other PRF Support, Statistical Team, Nurse Practitioner, and Study Team Medical Professionals.

Professional Hospital Interpreters: \$123,538

Interpreters needed 6.5 hours per day for 5 treatment days @ an average of \$55 per hour (fees vary from \$35-75 per language).

Translations of trial-related materials and phone interpreters: \$70,639

Based on 9 calls per child, and \$2,500 average per language for consent form and doctor letters.

Shipping (medications, original documents, etc.) and Supplies (Vials for blood and urine sample collection): \$46,007

Telephone (to discuss trial enrollment, travel logistics, and periodic check-ins with the families): \$10,742

Drug: \$0

Lonafarnib manufacturer Eiger Biopharmaceuticals is generously supplying the drug at no charge, and Everolimus manufacturer Novartis is generously doing the same.