FARA Friedreich's Ataxia Research Alliance

PRESS RELEASE

International collaboration advances gene therapy for Friedreich's ataxia

AAVLife aimed at advancing gene therapy for cardiomyopathy in Friedreich's ataxia to clinic

Downingtown, PA- April 6, 2014- The Friedreich's Ataxia Research Alliance (FARA) is pleased to recognize the ground-breaking gene-therapy research of FARA-funded scientist Dr. Hélène Puccio. In the current online issue of *Nature Medicine*, Dr. Puccio and her colleagues present significant results demonstrating that gene-replacement therapy using an adeno-associated virus to deliver the frataxin gene prevented and corrected cardiac damage in a Friedreich's Ataxia (FA) mouse model.[1] Based on these exciting and compelling results, a new company, AAVLife, has been founded with a clear commitment to the rapid development of a gene-therapy program focused on treating the life-threatening cardiac condition suffered by FA patients.[2] FARA has been collaborating closely with the founders of AAVLife since the middle of 2013 and with Dr. Puccio since FARA was first established in 1998.

Dr. Puccio, a research director at the French Institute of Health and Medical Research (INSERM), has been testing this gene-therapy approach in the cardiac FA mouse model that she developed in her lab at the Institut de Génétique Moléculaire et Cellulaire. The results show that a single intravenous injection of AAVrh10 expressing frataxin is not only capable of preventing the development of heart disease in the mouse, but also, fully and rapidly treats the mice with advanced stages of heart disease, returning the heart to normal function.

FA is a rare inherited condition that presents in early childhood with neurological symptoms, specifically loss of balance and coordination. However, it is progressive, leads to loss of the ability to walk and affects many other organs including heart, skeletal muscle and pancreas. The primary cause of early death, in the early 20's-30's, is a severe heart condition, cardiomyopathy.

FA is an excellent candidate for gene therapy because it is caused by a mutation in a single gene. Furthermore, this mutation is not in a coding region of the frataxin gene that codes for the frataxin protein. This means that, in individuals with FA, the frataxin protein is in

short supply but is perfectly formed and functional. Therefore, these individuals do not have to battle an abnormal protein and, if gene therapy can supplement the native gene with a new, correct gene that produces additional frataxin, the body should recognize the needed frataxin, should not mount an immune response to the supplemental frataxin protein, and should benefit significantly from a more normal supply of this important protein.

FARA's Scientific Advisory Board and Board of Directors have recognized that gene-therapy approaches would provide the opportunity for profound therapeutic benefit, and this area of research is a priority for the organization. Jennifer Farmer, Executive Director of FARA states, "When we first learned of Dr. Puccio's results and saw that she was demonstrating prevention and correction of the cardiomyopathy at both the functional and cellular levels we were beyond excited because this gave us evidence that we could attack the cardiomyopathy, which takes an individual's life at an early age. While we also want to have therapies that treat the neurological aspects of the disease, the significance of the cardiac disease is often under appreciated."

Mary Caruso, a founding director of FARA and mother of two young women with FA, remarks, "My girls have graduated from college and are pursuing productive lives in society despite significant physical disability. This is not easy. However, what scares me more than anything else is that the heart disease can advance at any time. My younger daughter, Alex has been rushed to the ER several times for heart symptoms and we watch her so closely. Results demonstrating cardiac improvement for FA strengthens the hope that so many families have been waiting and working for. It is the dedication of wonderful researchers like Dr. Puccio that keep our hope alive."

Ron Bartek, FARA President and co-founder added, "The launch of AAVLife and Dr. Puccio's tremendous achievement reported in *Nature Medicine* represent an exciting new opportunity for the FA community that comes from our international partnership. Dr. Puccio's research was funded by public agencies in France, Europe and the United States and AAVLife is bringing together international expertise and resources. This partnership is essential when we are battling a rare disease like FA. We are thrilled with the progress Dr. Puccio and her colleagues continue to make and are deeply heartened by the commitment of AAVLife. We know the company not only possesses sound business leadership and first-rate scientific talent but also works with the urgency felt by patients and their families. FARA will continue working closely with AAVLife, FA scientists and the patient community as, together, we drive this promising therapeutic approach forward into the clinic."

About FA

Friedreich's ataxia is a rare, degenerative, life-shortening neuro-muscular disorder that affects children and adults, and involves the loss of strength and coordination usually leading to wheelchair use; diminished vision, hearing and speech; scoliosis (curvature of the spine); increased risk of diabetes; and a life-threatening heart condition. There are no FDA-approved treatments.

About FARA
The Friedreich's Ataxia Research Alliance (FARA) is a 501(c)(3), non-profit, charitable organization dedicated to accelerating research leading to treatments and a cure for Friedreich's ataxia. www.CureFA.org

[1]The DOI for the paper as it appears online is 10.1038/nm.3510.
[2]AAVLife - www.aavlife.com

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