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Q&A with rare disease mom and biotech CEO Karen Aiach

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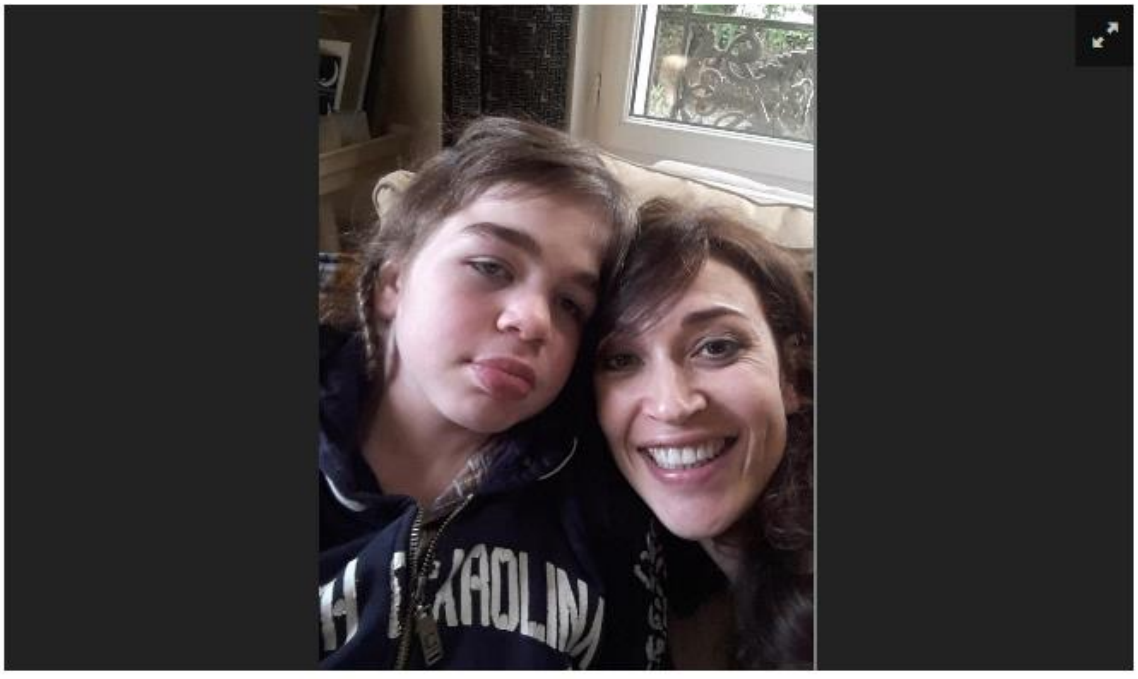

Karen Aiach, CEO of Lysogene, right, with her daughter, Ornella, who was born with... more

Karen Aiach worked for the accounting firm Arthur Andersen and then began her own consultant firm when, in 2005, her daughter was born with a rare neurodegenerative disease with no cure.

The resident of France started a foundation around the disease, called Sanfilippo Syndrome, but could not get a single company interested in a dedicated program to develop a drug for it. So she decided to start her own company in 2009 with the help of the former director of one of Europe's top gene therapy labs, Olivier Danos, who is now senior vice president of gene therapy research at Biogen (Nasdaq: BIIB).

Aiach, 44, is now the CEO of the French biotech Lysogene, which has 12 employees, has raised $30 million to date, and completed an early-stage trial of a treatment which replaces the gene that's defective in Sanfilippo patients. Lysogene recently opened a Kendall Square office with two employees, and is funding research and the University of Massachusetts Medical School into a treatment for another rare disease, called GM1 gangliosidosis.

This week, Aiach received a standing ovation as the keynote speaker at a conference hosted by Harvard Medical School called, "Precision Medicine 2016: Rogue Therapeutics." I interviewed her afterward about her decision to found a biotech company despite having no science background, and the advantages and disadvantages of being both a CEO of a drug company and a parent of a child with disabilities.

Tell me about this disease.

It's a neurological disease belonging to the family of lysosomal storage diseases. It is less well-known because there is no treatment, and is not really eligible for an enzyme replacement therapy approach because lysosomal enzymes are very big molecules and so if you (administer) them intravenously, they would not cross the blood-brain barrier. So that's probably the main reason why, when I had the diagnosis for my daughter, there was not a single company willing to

enter into a direct development for Sanfilippo Syndrome. As a lysosomal storage disease, Sanfilippo Syndrome is a monogenic disorder, so there is only one gene that is mutated, and because that gene is defective, there is an enzyme which is either absent in the body of the child, or is deficient. As a result of that, there is an accumulation of toxic substrates — in this case the substrates are sugars — and they will mostly accumulate in the brain, in the neurons, which leads to the neurological phenotype of the disease. On average the patients will not live beyond their teens.

It sounds like you must have been a doctor or in the medical field before this.

No, I am from a business background. I got my MBA from a major business school and started my career at (accounting firm) Arthur Andersen. I spent seven years, and then I had already created a small company. And when I had Ornella (in 2005), I was running that company. I didn't have any background in science or medicine, but I think in that particular situation, it maybe helped in a way, because the entry point of what I did was really to be motivated and save my daughter's life. There's nothing more that you need than really being passionate about it, and being driven to find a cure for your child.... Researchers were already, for some of them, involved in research on the disease, and my role was to really put all these people together and find money, and to organize a program which then became a company. So I believe actually with my background, it really helped putting a plan together and executing it.

How was the diagnosis process? I know for a lot of these rare diseases it can go on for years.

In the case of Sanfilippo Syndrome, because it belongs to the family of lysosomal storage diseases, there is probably a better awareness then for other diseases, because clinicians and physicians have known Gaucher, Fabry, Hunter and others for years. And if you look at a patient with Sanfilippo Syndrome, he or she will look a little bit like a Hunter patient. So when there is a problem, usually around

the age of 2, when they start deviating, cognitively speaking, from their peers, at one point they will normally necessarily be sent to a children's hospital, where there would be metabolicians, and in that this case, these guys would probably very rapidly put them under examination with urinary excretion measurements and enzyme activity detection and so on.... But in other cases, because of slight clinical features — she has a special face, a little bit like a Hunter's patient, with round nose and wide eyebrows — you may detect a patient with that type of diseases. And in the case of my daughter, she had a slight spleen enlargement at birth, and this is usually associated with LSD's.

How long did the whole process take?

It was very rapid in our case, because the pediatrician noticed the spleen enlargement at the first consultation, so one month after birth. And then he told us (to) put her under surveillance. At the age of 4-5 months, he said (we should) go to a metabolic team specializing in inborn errors of metabolism. And so from that point to the diagnosis, I think it was six or seven weeks. She was born in January 2005 and we had the diagnosis by the summer.

When did you make the decision to start a company rather that a foundation or any of the other things parents can do?

I first started with a foundation, actually, because this is a natural way of gathering and uniting when we are in this situation. But my point was really — because no one would do it — to put a therapeutic program together that I would lead, in which I would be the pilot. I think that this is what makes the difference. I was not looking for money to, you know, fund a team here, fund a team there, and see what happens. I made a sort of audit of what would be the right approaches, therapeutically speaking. And after having met with Olivier Danos, we came to the conclusion that what had to be done in that disease was gene transfer — gene therapy delivered directly into the brain. Once that was decided as the approach to be taken, my single purpose was to make it happen, and to make it happen according to my own rules in terms of timing, in terms of

independence. This is where I used my business background… I want the company to have the ownership of the data in order to be able to progress to a real drug development program, So I think that this is what makes the difference. I raised funding, went to the team, or teams, put money on the table and said, "This money goes with timelines and deliverables."

Why did you open an office in Cambridge?

We've already completed a Phase 1/2 study with our product, we've improved our product, and we are now preparing to new clinical studies with the new, optimized product…. In the U.S. we have our pre-IND meeting in one month. The Phase 1/2 was done in France with four patients, including my daughter. Results were published in 2013. We saw a very good progress in our patients with respect to behavior and hyperactivity, so that's great, because it's really meaningful for the parents and for the patients. The aim with the optimized product is to hopefully also make an impact on cognition in a situation where we would dose the patient earlier than what was done in the Phase 1/2. The next study will be a registrational study… with more sites in the trial. So we will have three or four sites in Europe, and one to two sites in the United States. So I believe this is a very good reason for us to have an office here in the country, to have early dialogue with the FDA, to have close contact with patient advocates here in the U.S., and to be close to the matter. Because we are not talking about administering a pill to patients, but really a neurosurgery, because the product is delivered via a two-hour surgical operation…. It's a very meticulous process we have to put in place, and I like to do that from here, when it comes to U.S. sites, rather than from Paris.

How many people are you expecting in this trial?

Twenty.

You have a partnership with the University of Massachusetts Medical School as well?

Yes, we are partnering with them to develop studies aiming at another lysosomal storage disease known as GM1 gangliosidosis. So we are funding research there in order to complete all the pre-clinical studies that we have to do with our vector, which is again an AAV-based product.

Are there advantages to being the CEO of a company, but with a unique interest in it because of you daughter?

The main advantage that we have as parents is we know the disease very well, and we know what is meaningful and what we should try to achieve in terms of clinical benefit to the patients. So it's not only about bringing a product to the market in accordance with the regulation, first and foremost, it's being able to have a product that will make a difference in patient's lives. And in order to do that, no one better than a parent can do it. A second advantage is, obviously we are passionate about what we are doing, and this is important in situations where we are pioneering science and medicine. Sometimes you feel a little bit alone, because you are a pioneer and the territory is unknown and sometimes unexplored. It's important then to be so motivated to face the fears that are associated with the unknown.

Does it help with investors, because they know your motive is pure and it's not all financial?

No, my daughter has been dosed. She was dosed in 2011, and I did my best as a parent. So now I'm really acting as the CEO of the company, with the goal to bring profitability to my investors and shareholders. That's why we are working so hard to put a registrational trial together that we aim at starting in the middle of next year, so hopefully we will reach the market at the beginning of the next decade. And we will advocate for the right price for that drug. The right price being the price that will combine our expectations in terms of profitability, but also the budget pressures than we know exist.

As a gene therapy, it would be a cure, right?

Yes. It would be life transformative — that's the minimum we can expect. In terms of pricing, our colleagues at bluebird, Spark, etc. are putting a lot of thinking into that, so we don't know yet where we will end up. But clearly, I think as a CEO, I aim at bringing money to the investors.

In biotech, obviously, most programs fail. How do you balance that, since because of your daughter, you emotionally want to see this succeed?

Yes, emotionally I want this to succeed. The main disadvantage of my position is probably emotion, but the other way around, in the sense that obviously there is an advantage in understanding the pains of families with children having GM1, or Sanfilippo. It helps in terms of sense of emergency, but at the same time this pressure is emotionally complicated for me sometimes. Because I already have to deal with my own life at home, and I have another child, etc. So sometimes that emotion is, yes, potentially difficult. And obviously my life at home is different from others, because I have a child with disabilities. It's not simple. Fortunately, I have a very nice board of directors, we have experts helping us.