When the doctor is not enough: The parents who became active researchers

John Crowley, CEO of Amicus Therapeutics, which develops drugs to treat rare diseases, represents a growing trend: Patients and their families are no longer satisfied with raising awareness of their illness or raising money for research. Instead, they are actively promoting research themselves.

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John Crowley, CEO, Amicus Therapeutics / Photo: PR

"Go enjoy the time you have left with your kids." That's what John Crowley was told at the end of a meeting with a specialist in rare genetic disorders. Crowley was a new dad, with an MBA from Harvard, working for a prestigious consulting company. Life looked good, and then, as the saying goes, it all came crashing down.

As far as the doctors were concerned, there was no dilemma here. Because there was no drug to treat Pompe disease, the illness that struck both of his children, there was no point wasting effort on treating them. The only thing to do was to make the children's lives as comfortable as possible during the coming period of decline.

Megan Crowley was fifteen months old and Patrick less than a month old when they were first diagnosed. The life expectancy of Pompe sufferers was then about two. The doctors prepared the parents for a difficult yet limited period.

Today, the two children are young adults aged 20 and 21. Their lives are far from perfect. They depend on respirators and in wheelchairs, but they are alive.

Thanks to intense multidisciplinary efforts on the part of Crowley, his wife Eileen, and their friends, as well as a community that sprang up around them, a commercial enterprise was built to start developing a drug to treat Pompe disease. Crowley, who headed the company, sold the project to Genzyme, the international biotech company, and managed the drug's development until it was possible to give the drug to his children. He succeeded in saving his children's lives and the lives of thousands more children. Some received the drug at an early stage, and they are doing better than Megan and Patrick.

Today, Crowley is CEO of Amicus Therapeutics, known in Israel mostly as Protalix Biotherapeutics' competitor in the treatment of Fabry disease. Amicus develops drugs for a range of rare diseases, not just Pompe. Crowley took a family crisis and made it his destiny. Now the company is traded on the NASDAQ and its value is assessed at $2.4 billion. Crowley feels that a company like this is the best chance for developing the next generation of drugs for Pompe as well as helping those affected by other genetic diseases.

How did your attitude differ from the attitude of other parents? And how did this attitude lead you to try the commercial route and manage a company?

"The very first night after getting the diagnosis, I sat in front of the computer and browsed the internet, which was still in its infancy (this was towards the end of the 1990s), and discovered that researchers at Duke were investigating the possibility of developing an enzyme that would replace the protein my children were missing because of their genetic mutation. I woke Eileen and told her, 'There's hope.'"

Crowley has said in the past that the family moved to New Jersey, which has a high concentration of geneticists, where he found work with the pharmaceutical giant Bristol Myers Squibb to study the drug development process. In the meantime, except for Bristol, the research into Pompe disease was going slowly, which is common in the industry, and, according to the literature, Megan only had a few months to live. She was extremely weak and hospital visits were becoming more frequent. Her life was in constant jeopardy. On a few occasions, Crowley found himself wondering if it wasn't best to put

an end to the suffering and let her go in peace. But, ultimately, the family and the doctors did not give up and again and again managed to stabilize the toddler. As this was going on, however, Patrick was starting to show the same symptoms as his sister.

In 2000, Crowley left his job with BMS to become CEO of Novozymes in Oklahoma. Novozymes was using the same initial research Crowley had read about on the internet. Utilizing other capabilities, it was working to develop a replacement of the enzyme. To help reach a fast solution, Crowley collected all the available research in the field which was being conducted in the United States, all which he became intimately familiar with from his extensive internet browsing.

Within a year, he had brought the company to such an advanced point,that it was bought by Genzyme. In the eighteen months in which he managed Novozymes, Crowley turned it from a startup of four to a fully functioning company with 120 employees all committed to the same goal - finding a drug to help Crowley's children.

After the $100 million buy-out, a sum now considered relatively low, Crowley continued to manage the division developing the Pompe drug within Genzyme. He made sure the work went rapidly thanks to unprecedented internal and external financing.

In 2003, it was already time for the drug's clinical trials at Genzyme. Crowley says he was accused of "a conflict of interest" (he won't say who made the accusation) when he asked that his children be among the first to receive the drug. In the end, he was forced to resign from Genzyme in order to enroll his children in the trials. They received their first treatment the same year and their medical condition started to improve.

After the drug was approved, Crowley - newly unemployed because of the situation with Genzyme - looked for a new management position in the biomed field. For a short time, he managed Orexigen Therapeutics, currently working to treat obesity, and was considering running for the New Jersey state senate, but in 2005 he rediscovered his destiny of putting his children first by joining Amicus as CEO.

Did you feel a certain discomfort in joining a company developing a competing drug to the one you developed and sold to Genzyme, the one that saved your children's lives?

Crowley is stunned by the question. "No. Genzyme, for commercial reasons, decided to develop a groundbreaking product, which gave it a great deal of commercial value. We are grateful to Genzyme, but there is so much more to do in the field and our job is to go and do it."

About two weeks ago, Amicus released the clinical results of an initial trial of a new drug for Pompe. Patients treated with the drug for eighteen months were able to walk farther than before; their muscles were stronger, and the levels of unwanted matter that accumulate in patients' muscles were lower. "These results are very meaningful. The drug passed the test of time in almost all the patients," said Crowley when the results were reported. "We want to bring the treatment to as many patients as possible, as fast as possible." In Crowley's case, these words are especially significant. The company hopes to begin a multi-locale clinical trial in which most Pompe sufferers willing to take the risk can participate before the end of the year.

Crowley was a pioneer, but the tendency of patients and patient families to seize the reins is not all that rare. Today, thanks to the internet, patients can access information relevant to their condition and learn as much about it as the professionals. Of course, it is not a simple process, but what the patients lack in professional knowledge and financial resources they make up for in dedication and sense of urgency.

Successes no longer a rarity

In the past, we interviewed Patrick Terry who sought to develop a drug to stop the progress of the genetic disease that would rob his two children of their eyesight and cause them to age prematurely. To do so, he became the CEO of Genomic Health Inc., a biotech company active in several fields, though it failed to find a drug to treat his children. We also spoke with Jonathan Silverstein, a senior leader of OrbiMed, a venture capital fund that scouts the globe for healthcare innovations. Silverstein was diagnosed with a genetically-based case of Parkinson's disease and founded a nonprofit to promote research into the disease.

In the past, patient nonprofits usually worked to raise awareness and capital to finance research. Today, the patients' battle is in pushing researchers and pharmaceutical developers to research their diseases and to do it fast. In addition, patients and their families are busy connecting researchers working in different locations, as Crowley did. Such connections can only help drug development. They also work to make medical information, such as genetic data, more accessible to doctors and researchers. Patients who succeed in building a genetic database or put together a group willing to be available at short notice for clinical trials, can make research into their condition more available and accessible to someone researching their illness, compared to a different disease, that may be better known in the literature or more common in the population.

There would seem to be competition between diseases, but most patients do not behave as if they are competing with one another, because breakthroughs can advance the whole field of research into rare genetic disorders and, later on, can have implications for the research of more common diseases not necessarily stemming from congenital genetic mutations.

To date, successes have not been frequent, but are also not as rare as they were in the past. Scientific innovations in the rare disease field and regulatory bodies' willingness to fast-track drugs of this type to clinical trials have definitely raised the odds in the patients' favor. The activist approach is becoming more worthwhile, although it requires a great deal of emotional and mental energy as well as time, and time is what these patients do not have.

The next stage: Healing the source and fixing the damaged gene

About a month ago, Galafold, the first Amicus product to treat Fabry disease, was approved for the U.S. market. Like Pompe, Fabry also involves a missing protein. The market leader, again, is Genzyme, the market pioneer, and for many years the only company selling a product to treat the disease in the United States.

In Europe, Genzyme shares the market with Shire and Israel's Protalix, which had planned on being number three in the market until Amicus overtook it. The product Amicus developed has a significant advantage in that it can be taken orally. In the past, Protalix claimed it is suitable only for some of the patients and is not a threat to its own leading product. Amicus, too, says the product is

suitable to patients with one type of mutation, representing some 30-50 percent of the market.

The products made by Genzyme, Shire, and Protalix all offer a replacement protein. When the drug was approved for use in Europe, before the FDA approved it for the U.S. market, it was approved for use in Israel and was added to the list of drugs covered by the national health insurance system. It is estimated that Israel has about 200 patients suffering from Fabry disease.

Today, the company is also working in the field of genetic therapy - fixing the miscoded gene responsible for the protein causing the disease. This would give hope that patients, if treated early enough, will be able to lead fully functional lives.

About a month ago, Amicus announced that, for $100 million (with the option of further payments in case of success), it had bought Celenex, a company with a portfolio of about a dozen genetic therapy treatments for various rare diseases. "This is really the next step in putting us in a place where I always hoped Amicus could be," says Crowley.

The transaction is a kind of a closing of a circle, because Gordon Gray, the founder and investor of the company that bought Amicus, has two daughter suffering from Batten disease, another rare genetic disorder. Gray was a Hollywood producer before his daughters got sick. In fact, he was considering buying the rights to make a movie about Crowley, who became an inspirational figure for him because of his own girls' situation. It was a contributing factor to his decision to establish and finance the company based on research being done at universities and research hospitals.

Had Amicus concentrated solely on Pompe and Celenex solely on Batten, this connection would probably never have been made. But both companies see their mission as much broader. This resulted in their synergy. Genetic therapies for both diseases will be developed at Amicus.