
Cystic Fibrosis Foundation

Straight talk with…
Robert Beall

'Venture philanthropy' has become a buzz term in the nonprofit sector over the past decade, but the concept was completely new to disease-focused charities when the Cystic Fibrosis Foundation decided to give it a try in 1998. Frustrated by the lack of progress toward targeted therapies for cystic fibrosis—a rare disease that afflicts just 70,000 people worldwide—Robert J. Beall, president and chief executive of the Bethesda, Maryland–based organization, added a bold new component to the foundation's research-funding strategy. Beall, who joined the foundation in 1980, launched a program aimed at absorbing the early financial risk involved in drug development as a way to entice for-profit companies to get involved in cystic fibrosis research.

That strategy was vindicated with the approval in January of the first small-molecule drug that directly interacts with the mutated protein responsible for cystic fibrosis. The drug, formerly known as VX-770 and now branded as Kalydeco (ivacaftor), has been a long time in the making. Yet all along the way there was Beall and his foundation, which has committed $315 million to for-profit companies for cystic fibrosis research over the years. **Elie Dolgin** spoke with Beall to learn more about his organization's pioneering approach to philanthropy.

What does this drug approval mean for people with cystic fibrosis?
It's a very exciting time for our community. For the patients with this mutation—the G551D mutation, which represents 4% of US patients—this is a life-changing event. But equally importantly, we've validated the science that small molecules can ultimately make a difference in the clinic. So, this will pave the way now for the other modifying drugs in people with other kinds of cystic fibrosis mutations as well.

What was the rationale behind going venture style in the late 1990s?
We had the gene. We had some targets. We understood the basic underlying defect. We had human cells, and we had indicator systems that could measure chloride levels. All these things could come together in a test tube, but it was taking academic scientists too long to do it. We had to accelerate the pace and bring industry in to that process, which meant we had to de-risk it. We had to take the early risk to draw them in.

Take me back to 1998. How did the collaboration between your foundation and Aurora Biosciences come about?
I felt, and some work in the laboratory had suggested, that we were ripe to do high-throughput screening of small molecules for cystic fibrosis. I approached several groups—not many people returned my phone call—but Aurora Biosciences agreed. They were a contract organization that had a technology platform involving gigantic robots that could do high-throughput screening. We started a small collaboration that we later expanded to $40 million to screen thousands of compounds a day. They were great technology wise, but we always say, "We'll give you the money, but four times a year we're going to meet with you face to face, and we're going to encourage you with milestones." It was a business relationship that we established. It wasn't a philanthropic relationship.

After Vertex Pharmaceuticals bought Aurora in 2001 and the lead compound moved into the clinic, how did the relationship evolve?
Vertex had the capabilities that a big pharmaceutical company has in terms of taking a clinical candidate and moving it forward, doing the toxicology and trying to make the compound into an oral drug. We then brought in more people who knew the clinical aspects of CF [cystic fibrosis], and we also gave them something else: we had a clinical trials network. I always felt that money was one thing, but no company is going to come to us if they can't do the clinical trials. So we started our own clinical trial network in 1998, rolled it out in 1999. We now have 40 staff members in Seattle who run and coordinate clinical trials for CF and a network of about 80 care centers around the country with an on-site coordinator who recruits for clinic trials.

How much money did the foundation invest in Aurora-Vertex?
Right now we have invested $75 million in bringing forward VX-770 and VX-809, which are currently being tested in combination in people with the most common CF mutation. In the last year, we also committed another $75 million to Vertex to accelerate the development of a backup to VX-809 and to look for new molecules that might be important as we move forward. That's not to say that VX-770 and VX-809 as a combination therapy aren't going to work, but we're not going to wait to find out.

With Kalydeco now on the market, how will the foundation recoup some of its investment?
We have royalty rights to the drug. We're going to take that money and invest it back into the research. This is not foreign to us, because we previously sold the rights to an antibiotic called TOBI that we developed and licensed to a company called PathoGenesis for $20 million, and last year we sold our rights to the enzyme therapy liprotamase to Eli Lilly. Every time we get these dollars, we put them back into research, and that's what our intention is to do now. That's why we've been able to expand our medical programs. In 2010 we spent $70 million; this year we're going to spend over $100 million.

Have other disease charities adopted the venture approach?
Many of them are moving toward this model—including the Multiple Myeloma Foundation, the Michael J. Fox Foundation [for Parkinson's Research], the Juvenile Diabetes Research Foundation and the Leukemia and Lymphoma Society—and we've been mentors for many of these groups. The fact is that many of these boards are seeing what's happened to the CF Foundation and are saying, "Why don't we do that?"