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*For the Southern California
Life Science Community*



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*At right: Lucia Santana,
checking compounds for purity
at Vertex Pharmaceutical's
San Diego facility.*

COVER STORY



FUNDING THE CURE:

FOUNDATIONS TREAD WHERE INVESTORS WON'T

by Larry M. Edwards

When Robert J. Beall picked up the phone and called Aurora Biosciences in 1998, he was looking for a miracle – not just in terms of a life-saving drug, but in the very process of how drug development is funded.

As the president and CEO of the nonprofit Cystic Fibrosis Foundation, he wanted to fund research at a for-profit company that he hoped would lead to a viable therapy, if not a cure, for those suffering from the deadly lung disease. But that funding model was unheard of at the time and could possibly endanger the foundation's nonprofit tax status. Today, Vertex

Above: Compounds under development at Isis Pharmaceuticals, which has research partnerships with several patient advocacy organizations.

Pharmaceuticals, which acquired San Diego-based Aurora Biosciences in 2001, has two compounds in clinical trials that hold the promise of extending the life expectancy of cystic fibrosis patients beyond the 37 years it is today.

“This CF project probably never would have happened under the traditional venture capital, entrepreneurial funding model,” said Paul Negulescu, vice president of research at Vertex's San Diego unit. “It was just too risky.”

But for Beall, CF patients and their families, “it was something we could not afford not to do.”

However, in the beginning even offering to fund research was not enough. Most companies still were not willing to consider that risk. Now that the concept has proven viable, it's a

different story. “Ten years ago, almost no one would return my calls,” Beall said. “Today, they are calling me with proposals, and I have to turn most of them down.”

NEW MODEL GAINS TRACTION

The CF Foundation model, known as venture philanthropy, has been duplicated by a number of patient advocacy groups, several of which have funded research in Southern California life science companies. While the concept of venture philanthropy has been around for some time, Beall spun it in a new direction, using funds from a nonprofit health charity to underwrite research by for-profit life science companies. In addition to Vertex, these include SGX Pharmaceuticals Inc., Hollis-Eden Pharmaceuticals, Ceregene Inc., Isis Pharmaceuticals Inc., Active-Sight, Nereus Pharmaceuticals, Novocell Inc. and GenPathway Inc. in San Diego and CytRx Corp. in Los Angeles.

Nationwide, according to *CenterWatch Weekly*, an industry newsletter, U.S. disease foundations invested about \$75 million in 2007 in biotech companies, a tenfold increase since 2000. At \$48 million, the CF Foundation claims the lion's share of that investment and continues to spend more on

drug research than any other disease foundation in the country.

The other major players in this form of venture philanthropy (based on 2007 investments) include: Juvenile Diabetes Research Foundation, \$14 million; Michael J. Fox Foundation for Parkinson's Research, \$4.6 million; Muscular Dystrophy Association, \$3 million to \$4 million; and Multiple Myeloma Research Foundation, \$2 million to \$3 million.

Beall, and those who have followed his lead, say the concept was born of frustration. "By 1998, we knew what the problem was with the gene, but biotechnology companies were not interested, and there was no government support," he said. "So, the question was, how do we get companies involved with us?" That's when he began making cold calls.

One of the few companies to respond was Aurora Biosciences, which had a platform for high-throughput screening, and they struck a deal. When Vertex acquired Aurora, the research program continued and led to the development of the compound VX-770, now in a Phase 2 clinical trial. A second compound, VX-809, is in a Phase 1 clinical trial. Current therapy involves lengthy daily rituals of inhaled medications and physical therapy. If Vertex's compounds become viable,

they could allow CF patients to take a pill as part of their CF treatment regimen.

For Vertex, it's a "win-win" collaboration, Negulescu said. "The CF Foundation paid for most of the research, so there was no real downside for us."

Michael Grey, the CEO of SGX Pharmaceuticals (formerly Structural GenomiX), expressed similar thoughts. The company's relationship with the CF Foundation began in early 2001 and is ongoing – at about \$3 million a year – as researchers continue to identify the structural characteristics of the defective CFTR protein.

"This is early-stage, pre-competitive research traditionally done within academia," Grey said. "But SGX, with its throughput screening capabilities, is a better place to do this fundamental research. The timeline is accelerated."

THE ART OF THE DEAL

The downside within a for-profit company, Grey explained, is committing resources when the returns are long-term. Nonetheless, the value to SGX goes beyond the funding, he said, because "this is the most challenging thing we do, and we gain insights in structural biology that help us in other



Sample-testing machinery at Isis Pharmaceuticals.

areas of drug discovery."

It's that accelerated timeline that led Beall, in 2000, to establish the Cystic Fibrosis Foundation Therapeutics Inc. as a nonprofit drug discovery and development affiliate of the CF Foundation. Since then, the CFFT has become a virtual biotech with 13 therapeutics in its pipeline. In the past decade, the organization has pumped nearly \$300 million into biotech companies nationwide, with about \$75 million of that going to three firms with Southern California ties: Vertex, SGX and Hollis-Eden.

But unlike traditional venture funding, when a drug is commercialized under this model, the foundation's



Mekoya Albe, handling compounds for testing at Vertex Pharmaceutical's San Diego facility. Vertex has received more than \$70 million in funding from the Cystic Fibrosis foundation.

intellectual property rights are sold immediately, and the monetary benefit is channeled back into more research. “We don’t want there to be any appearance of a conflict of interest,” Beall said.

The Michael J. Fox Foundation for Parkinson’s Research has fashioned its “clinical discovery” approach on the CFFT model, but chief executive officer Katie Hood takes the venture philanthropy label a step farther. “We call it ‘disruptive philanthropy,’ because we are not accepting the normal role of a foundation,” she said. “We do whatever it takes.”

In 2004, Hood learned about Ceregene, which is focused on the development of gene therapies for neurodegenerative disorders. The company’s Phase I clinical study of

CERE-120 had shown potential in preclinical testing to slow or stop the progression of Parkinson’s disease. The foundation stepped in to accelerate the optimization of clinical tests for the therapy.

“Our goal is to change the risk paradigm for entrepreneurs and private companies,” Hood said.

MJFF has worked with 28 companies, committing \$21 million to collaborative projects with for-profit companies out of \$115 million in research funding. Hood said there is no conflict of interest because all projects are peer-reviewed and the foundation does not take an equity stake in the company or intellectual property rights. However, the foundation does benefit through the retention of continuation rights, should one partner bow out, and “pay-back rights,” under which the foundation is reimbursed for its funding if a therapy is commercialized.

Isis is also conducting research related to neurodegenerative diseases with funding from nonprofit foundations: CHDI Inc., which is pursuing treatments for Huntington’s Disease, and the ALS Association, which is seeking treatments for amyotrophic lateral sclerosis, commonly called Lou Gehrig’s disease.

THE FUNDED

Some Southern California life science companies with direct funding from patient advocacy organizations:

- ActiveSight has collaborated with the CHDI to study drug targets for Huntington’s Disease.
- The Juvenile Diabetes Research Foundation has donated more than \$1.16 billion to diabetes research and is currently funding trials of Amylin Pharmaceutical’s diabetes drugs.
- Ceregene has received more than \$1.9 million from the Michael J. Fox foundation to study its gene-therapy drug to treat Parkinson’s disease.
- CytRx has received \$24.5 million from the ALS Charitable Remainder Trust to study ALS.
- Hollis-Eden Pharmaceuticals has received more than \$2 million in funding from the Cystic Fibrosis Foundation to study potential treatments for cystic fibrosis.
- Isis Pharmaceuticals has an agreement with the CHDI for up to \$9.9 million in funding to study using antisense drugs on Huntington’s disease.
- Isis also has received funding from the ALS Association and the Muscular Dystrophy Association for the study of an antisense drug to treat ALS.
- Nanogen is part of a team that has received \$15.4 million in funding from the Bill & Melinda Gates Foundation for disease diagnostics in developing countries.
- Nereus Pharmaceuticals is working with the Multiple Myeloma Research Foundation and has a product to treat Multiple Myeloma in clinical trials.
- Novocell has received funding from the Juvenile Diabetes Research Foundation to look at new treatments for Type 1 diabetes.
- The Cystic Fibrosis Foundation has also pledged up to \$15 million to SGX Pharmaceuticals to study potential treatments for cystic fibrosis.
- Vertex Pharmaceuticals has received \$79 million in funding from the Cystic Fibrosis Foundation and has two products in clinical trials resulting from this collaboration.

In October 2007, the company inked a three-year, \$9.9 million deal with CHDI for the discovery and development of an antisense drug for the treatment of HD. The partnership is ideal,” said Isis executive vice president Jeffrey M. Jonas. “The organization has a mission to treat a rare but important disease, and Isis has technology adept at rapidly and efficiently developing a drug that can strike at the molecular mechanism of the disease.”

Upon completion of IND-enabling studies, Isis and CHDI will continue to collaborate to ensure that any resulting drugs will be broadly available to HD patients, and Isis has the right to continue clinical development of those drugs arising from the collaboration. The agreement with the ALS foundation is similar.

Los Angeles-based CytRx Corp. has a deal with the ALS Association as well. In 2006, the company signed a \$24.5 million royalty agreement with the ALS Charitable Remainder Trust to fund continued development of the company’s lead small-molecule drug candidate, arimoclomol.

FILLING A FUNDING GAP

Patient advocacy groups will play an increasing role in funding commercial



Aaron Williams, operating screening robotics at Vertex San Diego, which is developing two drugs for cystic fibrosis.

research in the coming years, according to Jonas. “As the regulatory environment becomes more onerous, groups with a particular interest will drive research, because pharmaceutical companies make investment decisions based on market size or the ease of regulatory approval, not on a project’s scientific or medical merits,” he said.

In addition, these groups are typically affiliated with medical facilities, providing access to research experts and sites for clinical trials. The CFFT has its own clinical trials network and enrolls patients in trials for new CF therapies, such as those being developed by Vertex.

Providing this base of support, not only in funding but also infrastructure,

has proved invaluable in enlisting private companies to conduct research and development projects they would otherwise deem too risky.

“We would not have started this project, or continued its development, without the support of the CF Foundation,” said Vertex’s Negulescu, adding that his company is open to using the venture philanthropy model to fund other projects. “It has been a good experience. We would do it again.”

Larry Edwards is a senior writer with Cook & Schmid. For more information, go to www.cookandschmid.com.

Vertex photos courtesy of Mike Weymouth of Weymouth Design and Vertex Pharmaceuticals.