

FIERCEBIOTECH SPECIAL REPORT

FOUNDATIONS FUEL RISKY BIOTECH VENTURES

BY ARLENE WEINTRAUB



When Gaithersburg, Md.-based Amplimmune announced on Jan. 7 that it had formed a \$50 million research alliance with Japanese pharmaceutical giant Daiichi Sankyo (\$DSKYF), it was more than just a victory for the 6-year-old biotech company. It was also a validation of the approach taken by the National Multiple Sclerosis Society's Fast Forward Fund, which in 2009 invested \$500,000 into the development of the Amplimmune drug at the center of the Daiichi deal, AMP-110.

"Fast Forward really laid the groundwork for the early chapters of the [AMP-110] story," says Michael Richman, Amplimmune's CEO. "The MS Society linked us up with experts to help us answer key questions about the molecule and how it's functioning. That de-risked the program. Now Daiichi Sankyo will take it into clinical development."

Non-profit, patient-focused foundations are becoming an increasingly visible force in early-stage biotech research. And they're not just handing out grants to academic scientists and hoping the discoveries they fund someday make it into clinical practice. Today's philanthropic financiers are being far more proactive—funding biotech companies through early-stage clinical trials, for example, or providing capital for entrepreneurs to take discoveries out of academia and translate them into commercial opportunities.

Foundations are investing in biotech research because of a common goal to speed up the translation of discoveries into useful products for patients. That means funding risky, early-stage clinical trials that venture capitalists won't touch, or developing therapeutic ideas that cash-strapped startups don't have the resources to pursue. "The benefit of being a nonprofit is that, unlike a biotech startup—which would be forced to focus on its top priority, or maybe its top two—we want to have as many compounds moving forward as possible, with as many different partners as possible," says Scott Johnson, founder of Saratoga, CA-based Myelin Repair Foundation (MRF), which is focused on finding new drugs to fight the disease he suffers from, multiple sclerosis.

Washington, D.C.-based FasterCures, which is an advocate for accelerating research, lists more than 50 nonprofits that are currently working with companies on research projects. They range from large organizations such as the New York-based Juvenile Diabetes Research Foundation and the Multiple

Myeloma Research Foundation in Norwalk, CT, to smaller groups, such as Parent Project Muscular Dystrophy in Hackensack, NJ.

This brand of venture philanthropy is poised for tremendous growth, predicts Peter Lomedico, director of industry partnerships and cure therapies for the Juvenile Diabetes Research Foundation (JDRF), which launched a formal effort to partner with companies in 2004. "We're trying to achieve catalytic events," Lomedico says. "We're accelerating research may not have otherwise happened."

Since launching its industry-partnering program in 2004, JDRF has poured \$110 million into more than 40 companies, and has partnered with Big Pharma leaders such as Pfizer (PFE), Eli Lilly (LLY), and Sanofi (SNY) to advance early-stage science in diabetes. Now other foundations are following JDRF's lead, Lomedico says. "In the beginning it was just us and a couple of others, but now I get calls all the time from other foundations looking for advice on how to set up industry partnerships."

Another foundation that's embracing venture philanthropy is the New York-based National Multiple Sclerosis Society, which launched its investment fund in 2007. The fund, called Fast Forward, has invested about \$15 million so far in early-stage MS research, and is looking to deploy another \$3 million to \$5 million this year, says Timothy Coetzee, president of Fast Forward.

One way foundation-managed funds differ from traditional venture capital is that non-profits are motivated more by the need to find cures than they are by the promise of making a financial return, Coetzee says. "Our limited partners are the people with the disease, and the ultimate return will be treatments or diagnostics that clinicians can use," he says. "We believe very deeply that if we don't make investments, who will?"

Coetzee first got wind of Amplimmune at the JP Morgan Healthcare conference in 2008, and he asked the company's CEO, Michael Richman, to send him a proposal. One of Amplimmune's experimental biologics, AMP-110, was designed to modulate the immune system to reduce the proliferation of



inflammatory cells and decrease the expression of pro-inflammatory proteins. But its exact mechanism of action wasn't clear. "We were very specific in saying some of the plan that they were putting forward was interesting, but it really needed scientific help," Coetzee recalls.

So in addition to investing in the drug, the MS Society hooked Amplimmune up with Stephen Miller, a researcher at Northwestern University who specializes in immune models of MS. As a result of that collaboration, Richman says, "We were able to design the appropriate studies to get a better understanding of what this molecule was doing, but also how it could be applied."

Amplimmune is examining AMP-110's potential in several autoimmune diseases. Daiichi Sankyo has not yet announced which indication it plans to pursue under the recently announced deal. And while the MS Society did not broker the Daiichi Sankyo deal, Richman says he believes Fast Forward's guidance nudged AMP-110 to the point where it could garner interest from a major pharma company. "It laid the groundwork for the early chapters of the story," Richman says. "Fast Forward's support was instrumental in putting this on a critical path towards the clinic."

More than Money

Amplimmune is just one example how not-

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for-profits can offer benefits to biotech projects that extend beyond the funding, Coetzee says. "We bring informal pieces, like advice about what outcome measures might be needed in clinical trials, or which clinical experts [companies] should bring to the table," he says. "Sometimes it's less about the money and more about the relationships."

Sharon Hesterlee, vice president of research for Parent Project Muscular Dystrophy (PPMD), says the connections that non-profits have to the medical and funding community at large can be vital for startups. PPMD, for example, regularly talks to venture capitalists and Big Pharma companies about opportunities in muscular dystrophy, she says.

It was PPMD's close relationship with its bigger-name cousin, the Muscular Dystrophy Association (MDA) in Tucson, Ariz., that really paid off for Tivorsan, a Providence, R.I.-based biotech startup developing biglycan, a protein that has been shown to help stabilize the muscle cells that degenerate in children with Duchenne Muscular Dystrophy. PPMD invested \$565,000 in Tivorsan in 2012, which was closely followed by a \$1 million grant from MDA. Together the two organizations are collaborating to dole out the payments according to research milestones, Hesterlee says.

PPMD has worked hard to shepherd biglycan out of academia. In 2008, the organization provided a \$289,000 research grant to Justin Fallon, the Brown University scientist who was developing the molecule. "When he started moving this along the direction of drug development and founded [Tivorsan], it was natural for the company to come to us for funding," Hesterlee says.

As part of that funding commitment, PPMD put Tivorsan through a rigorous scientific

review process that CEO Joel Braunstein says was essential for solidifying a business plan that would ultimately resonate with venture capitalists. PPMD connected Tivorsan with a non-profit group in Europe called Treat-NMD, an independent group of academics and industry leaders who reviewed Tivorsan's scientific plan.

In addition to filling out a lengthy application, Tivorsan's team had to sit in front of the Treat-NMD committee for several hours and answer questions about the program.

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The company and Fallon's lab have generated support from a number of other nonprofits focused on muscular dystrophy, including Stockbridge, MA-based Charley's Fund and the Nash Avery Foundation in Minneapolis. "Tivorsan has done a very nice job of traversing the Valley of Death, by leveraging a number of different sources of support," Braunstein says.

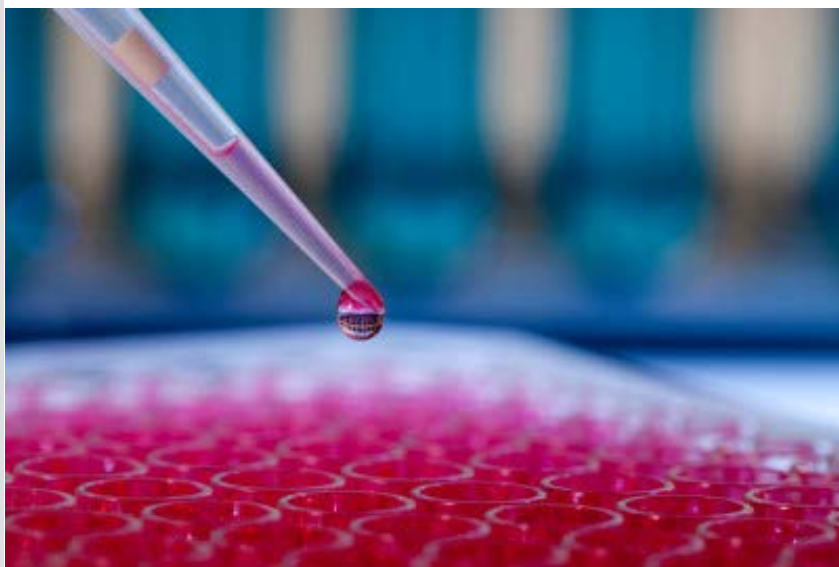
The company is currently working on a venture financing round, a process that Braunstein says has been enhanced by Tivorsan's close connections to patient-advocacy groups. "The foundations offered not just privileged access to the patient community, but also to key opinion leaders," Braunstein

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says. "For a new company getting off the ground, those additional relationships can be very helpful."

Funding to Inflection Points

Most managers of non-profit venture funds share a common goal: to support early-stage research to a point where



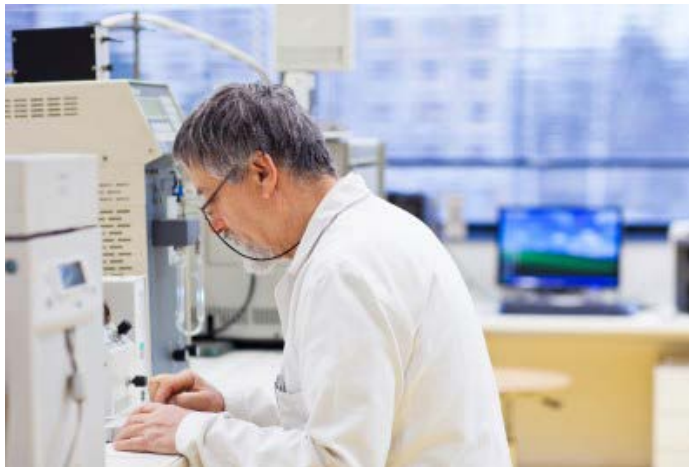
they can hand the programs off to deep-pocketed investors. Sometimes that means funding a company through a proof-of-concept study. In the case of Tivorsan, Hesterlee says, PPMD would like to support the startup through its filing of an Investigational New Drug (IND) application to the FDA. "We're trying to bring them to that certain inflection point,"

Hesterlee says. "They need money to get there."

The Leukemia and Lymphoma Society (LLS) also has a goal of funding companies to key handoff points, and it recently recruited an important ally in that task: biopharma giant Celgene (\$CELG). Last October, the White Plains, NY-based LLS said that Celgene would partner with the society to identify and speed up the development of new therapies for blood cancers. Although the financial specifics of the deal were not announced, says Richard Winneker, senior vice president of research for LLS, "as a result of their support, we can fund more academic research. We can potentially invest in more companies." In return, Celgene will be given the right to first negotiation for any deal involving a molecule it has funded, he says.

Celgene is the first company to sign on for a new LLS program called "Targets, Leads and Candidates." The initiative is aimed at identifying and funding priorities in research, with the support of biotech and pharma companies. "Our history has been about committing a large percentage of our dollars to academic research," Winneker says. "In order for that work to better translate into assets of interest to the pharmaceutical industry, we created a program through which pharma companies can provide their advice and financial support."

Celgene was a natural fit. The Summit, NJ-based company had already formed some valuable alliances with companies that LLS was supporting, namely the Boston-area oncology drug developers Avila and Epizyme. In January 2012, Celgene bought Avila for \$350 million, plus the potential for \$575 million in milestone payments. Four months later, Celgene partnered with Epizyme to develop cancer therapies based on the startup's work



in epigenetics. Epizyme got \$90 million up front and the promise of up to \$160 million in milestone payments. (Celgene did not respond to requests for comment.)

Jason Rhodes, executive vice president and chief business officer of Epizyme, says early support from LLS was critical for proving the potential therapeutic benefit of the molecule at the center of the Celgene deal, EPZ-5676. The drug targets an aberrant gene called DOTL1, which drives the growth of a rare cancer called mixed lineage leukemia. In 2011, LLS committed \$7.5 million towards getting the DOTL1 program through Phase 1 testing. "That was a really significant commitment to a young company," Rhodes says. "Having the LLS for both financial and strategic support was really critical for making that program a priority for us."

LLS sometimes funds late-stage drug development programs, if the organization believes it can speed up the process of moving promising molecules closer to the market. In 2010, for example, the society vowed up to \$10 million to support a Phase 3, multicenter trial of a drug called rigosertib, which Newtown, PA-based Onconova was developing to treat rare cancers. "The scope of the trial was too large for a small company like ours to do by itself," says Ramesh Kumar, CEO of Onconova. With the funding, Onconova was able to expand the trial from one site to 88, he says.

Then, last September, Deerfield, IL-based Baxter International (\$BAX) struck a deal with Onconova worth up to \$565 million for European rights to rigosertib. Though the need for LLS's funding has diminished, Kumar says Onconova continues to find value in the society's support. "The money is the least important of the benefits," he says. "They direct patients to clinical trials. And they are a very

high-profile group. A small company being associated with them adds a lot to our profile.”

Making Nonprofit a Business

The nonprofit world has become so important in life sciences that entirely new business models are forming around the idea of funding early research with the primary goal of generating new drugs—not financial returns.

In 2010, for example, Charley’s Fund and Nash Avery Foundation teamed up to launch Dart Therapeutics, a Cambridge, MA-based company that’s entirely focused on developing drugs to treat Duchenne Muscular Dystrophy (DMD). Its two lead candidates are small molecules, but Dart chairman and CEO Gene Williams says Dart is “looking at the whole spectrum—small molecules, peptides, proteins. The costs of manufacturing large molecules can be daunting, but if it’s an effective therapy, we will find a way to get it done.”

Dart’s strategy is to blend venture philanthropy with investor capital in a measured way. “We offer an investor syndicate a hyper-virtual, extremely leveraged capital structure,” Williams says. “We’re hyper-virtual because the overhead costs are covered by sustaining donors. What makes it leveraged is we get 20% to 40% of the funding for any program from the foundations. Those foundations are looking for a return of capital but usually its modest—say a 15% return, only upon success. Therefore it’s friendly capital that we can use to de-risk the asset.”

Another priority of nonprofit-backed startups is to speed up the drug development process. Towards that end, the Myelin Repair Foundation, founded in 2004 by MS patient Johnson, has funded the development of assays and other tools that can be used to test the

ability of experimental compounds to rebuild the protective myelin coating around nerve cells.

After years of relying on contract research organizations to run the tests, the foundation opened its own lab in January 2012. “We moved some of the assays we’ve funded into our own lab, so we can run them at higher throughput and with more consistency,” Johnson says. Veterans of Amgen (\$AMGN) are running the lab, which MRF calls the Translational Medicine Center.

Johnson says the MRF has already gotten requests from biotech companies that want to learn if their compounds might work against MS. “They want to get better answers faster, and were willing to pay to get their compounds evaluated,” he says.

Although the funding models may differ from organization to organization, virtually everyone agrees that the ties between the biotech industry and nonprofit patient-centered organizations will only continue to strengthen. “As more and more foundations think through it, they see the logic,” says the JDRF’s Lomedico. “To get advances out of the clinic and into the marketplace you really need to be working with companies.”

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