

Stanford SOCIAL INNOVATION^{Review}

Supplement
Eyes Wide Open
By Dennis Price

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Root's new business plan now speaks of "moderate" growth.

With Root Capital's disbursements in Africa more than \$47 million in 2015 and the firm on track to repay the Gates Foundation's loan, the investment itself has been a success. All told, in 2015 Root disbursed \$154 million to 277 businesses, which the lender claims generated \$1.2 billion in total revenue, the bulk of which was paid directly to agricultural producers

"It's no longer Root's goal to simply grow," says Gill. "There is a relationship between growth and ability to lead, but it need not be fast. In the end, you can't be all things to all people."

To Rossow, the question was never about Root Capital's dedication to the mission. Stronger financial controls, he felt, would enable the organization to be successful, to demonstrate the model, and to expand access to capital for smallholder farmers worldwide. Failure would undermine Root as a model for others.

"There's this tension between growth and good governance," says Rossow. "Organizations with a social mission must aim to be financially responsible. Without a financial success story, there's no social success."

Finding the right blend of toughness and love in its relationship with Root Capital was the Gates Foundation's biggest challenge. Sitting back and ignoring the breach would have been irresponsible, given the role the foundation seeks to play as a lender and as a partner to Root. Being too heavy-handed and directive risked overstepping its role. The key, in the end, was to be consistent with its goals from the start, build a strong relationship with Root, and let the organization drive the changes.

"Playing a catalytic role in driving internal change? That's more valuable than our capital," says Rossow. "We could have pulled our cash. We could have told them how to run their business. We were impressed with how seriously they took our pushback. It became a board issue. They put resources against a plan."

Gill, meanwhile, has come to appreciate the Gates Foundation's clarity and discipline. "The Gates Foundation's aim is to crowd in capital, demonstrate the model, and achieve a proof point," she says. "They pushed on us hard and at a very interesting time for our organization. I believe we are the better for it." ♦

Eyes Wide Open

Good reasons for a bad investment in a low-cost HIV test.

BY DENNIS PRICE

Here's a riddle: When is a bad investment a good idea?

In 2011, the Bill and Melinda Gates Foundation made a \$10 million loan to a biotech startup with a potential breakthrough product—and a high likelihood of financial failure. On the basis of promising scientific progress, it made another \$6 million loan a year later, with similarly low expectations of financial success. And even when the company was on the verge of insolvency in 2014, the foundation provided an additional \$356,000 to keep the lights on for two more weeks. All that was in addition to \$7 million in grant money.

In all, the Gates Foundation poured roughly \$23.5 million into Fremont, Calif.-based Zyomyx Inc., which went out of business before it ever delivered on its considerable potential for global health gains.

The reasons behind the willingness of the world's largest foundation to continue to invest in a declining company illuminate both the promise and the peril in using philanthropic dollars to back high-risk startups with the potential for significant social benefit. Mindful of the lessons from the failure of its investment in Zyomyx, the Gates Foundation team has since made 13 other program-related investments in biotech startups, totaling \$167 million.

Members of the Gates Foundation in-house investment team do not quite embrace the *en vogue* notion that failure is good. Rather, they say they knew at the time that Zyomyx had a high likelihood of financial failure without considerable additional investment by the foundation. They went ahead anyway, because the potential social impact outweighed the financial risks. As it happened, the company failed to deliver. Even the foundation's team of scientists and

investment professionals couldn't rescue a struggling company in a difficult market.

The prize worth the risk of failure was Zyomyx's HIV test. As a way to count CD4, or T-cells, in the blood, the test promised to cost a fraction of other methods for determining when to initiate antiretroviral treatment. Because Zyomyx's test did not rely on electricity or highly trained personnel, it was considered a critical link in a broader strategy to decentralize HIV treatment and expand access to treatment for tens of millions of poor people living with the disease.

The Gates Foundation's dogged effort to bring the game-changing product to market started with a loan to a company that commercial investors wouldn't touch. The \$10 million secured loan gave the foundation certain rights to the company's assets—including intellectual property rights—in case of a bankruptcy. That the march of science and a changing marketplace mean that Zyomyx's patents and processes are not so valuable to the achievement of the foundation's objectives after all only sharpens the investment's lessons.

BLOOD TESTS

An affordable and easy-to-use HIV test had been a Gates Foundation priority as early as 2005. That year, more than 33 million people worldwide were living with HIV, more than two-thirds of them in sub-Saharan Africa.

The "cocktail" of antiretroviral therapy, or ART, has been a lifesaver for people living with AIDS. At the time, such treatment reached fewer than half of those eligible for treatment in low- and middle-income countries. World Health Organization (WHO) guidelines targeted treatment to the sickest.

Because it was difficult to assess a patient's viral load directly, doctors instead looked at the specific white blood cells the virus targeted. The most effective way to identify the progression of the disease was

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to count the presence of CD4 cells in patients' blood. The more CD4, or T-cells, the less the disease had progressed. In 2010 WHO mandated treatment only when the CD4 count had fallen below 350.

"There was simply not enough money to fund the treatment required," says Christine Rousseau, a senior program officer on the Gates Foundation's HIV team. The difficulty of figuring out who should get the rationed cocktails made a simple, low-cost test an urgent necessity.

Existing CD4 tests were expensive and required electricity. Local clinics couldn't process blood samples. Patients were required to travel to larger facilities to take the test, then return weeks later for the results. More than half the patients never returned for the results and therefore were never enrolled for antiretroviral treatment, even if they qualified.

In 2005, the Gates Foundation and the Imperial College London launched the CD4 Initiative, a five-year, \$16 million challenge to create a CD4 diagnostic test that was easy to administer and low cost. Five organizations were awarded funds to test different approaches. By 2009, Zyomyx's test was the only one that met the initiative's specifications.

In less than 10 minutes and using no electricity, Zyomyx's test could separate and count CD4 cells in a drop of blood. Minimally trained health workers could read the tiny glass tube like a thermometer. Results could be relayed to patients as they waited. If manufactured in the millions, the cost per test would be reduced to \$6 (other available tests cost \$8 to \$15). The Clinton Health Access Initiative, a project of former president Bill Clinton's charitable foundation, estimated that there was demand for as many as 7.5 million point-of-care CD4 HIV diagnostics tests per year.

For HIV patients in poor, rural communities, the Zyomyx test could be life saving. For the global health community, it could be game changing, saving about \$130 million a year and accelerating the scaling up of critical antiretroviral therapy. "Zyomyx's new test will have a huge impact for people living with HIV across the world," Dr. Hans-Georg Batz, director and co-founder of the CD4 Initiative, said in 2009.

"Now that we have achieved this significant milestone, we are actively engaging with select global sales and distribution partners who can help us take the Zyomyx

test to market," added Zyomyx CEO Peter Wagner when the CD4 Initiative selected his firm's product as the top-performing test. At the time, the company estimated that it would take another \$25 million to bring the unproven HIV test to market across sub-Saharan Africa. Private investors weren't interested.

NEW TOOLS

Investments by philanthropic foundations in for-profit startups were novel five years ago, and they still are. To the extent they determine that the private sector holds needed know-how, foundations typically either contract for existing drugs and products or make grants to labs to get the technology into the hands of global health professionals.

The Gates Foundation, which in the 2000s became one of the world's largest funders of global health initiatives, had done all those things. By 2011, it was ready to try a new tool. Two years earlier, the foundation had set aside \$400 million on its enormous balance sheet to make program-related investments (PRIs), including loans, volume guarantees, and equity investments, to further its strategic goals in global health, education, agriculture, and other areas. The foundation later increased its PRI mandate to \$1.5 billion.

The Gates Foundation hired Julie Sunderland, formerly head of Oriane Consulting, to direct its PRI program. Sunderland's new team of former investors and bankers, tasked with making PRIs to finance market-based projects, took guidance on which projects to fund (and what rights were required to achieve the foundation's charitable objectives) from the foundation's program teams of scientists, academics, and development experts.

Few other foundations were investing actively alongside private investors in biotech startups. That scenario was only recently added to the illustrative examples of PRIs that the US Internal Revenue Service provides to foundations. Even at the foundation, few program officers wanted to work with for-profit companies.

Zyomyx was the first deal the foundation's HIV diagnostics initiative brought to the new strategic investment team. The company's underlying technology had other valuable applications for assessing total white blood cell count, CD8 counting, and blood typing.

But in the hard-nosed venture capital-

ist appraisal that the Gates Foundation PRI team was charged with making, Zyomyx's financial prospects were bleak. Zyomyx was still in the early stages of testing the CD4 test. Even if it nailed the product's development, commercializing it was going to be difficult. With any sales targeted at poor people in poor countries, the PRI team couldn't see a break-even point even if Zyomyx overcame the scientific and regulatory challenges and brought the new test to market.

"It is clear from the valuation analysis that this is not a rational investment from a financial perspective and that foundation should expect to lose all its money," Gates Foundation program investment officers wrote in their 2011 memo to the foundation's Investment Committee.

The only way the low-cost CD4 test was going to come to market was for the foundation to provide the cash. The Gates Foundation's HIV team, accustomed to providing grants, were willing to fund the development costs fully, with no expectation of a financial return.

RISK SHARING

The simplest solution would have seemed to be to fund the CD4 work with a traditional grant. But with the company so shaky, the Gates Foundation team felt that it was crucial to understand what would happen to the technology if the company went bust or, perhaps more likely, shifted its attention to more commercial products and markets. Grantees that violate their grant agreements can be made to repay the amount of the grant. The foundation wanted something more: a structure that would allow it to secure rights to the critical intellectual property.

The financing was structured as a loan, with Zyomyx's patents as collateral. If the company went bankrupt the foundation would gain control of the intellectual property ahead of other investors.

One test of whether a deal qualifies as a PRI for tax purposes is whether other investors would participate on the same terms. Making a \$10 million loan to a risky startup is certainly a risk few commercial lenders would take.

To ensure that the investment furthered the foundation's charitable goals, and to avoid excess private benefit, the Gates Foundation team structured an agreement that required the product to reach the very

poorest people affected by HIV. The agreement capped the amount of profit Zyomyx could make on tests sold in developing markets, potentially lowering the company's appeal to future investors.

The Gates Foundation's loans were structured as convertible notes that would convert to equity if Zyomyx found additional investors, was acquired, or went public in an IPO. In the unlikely upside scenario in which Zyomyx became a success, the equity stake would give the foundation lever-

that the entire amount of the investment should come from the program team. The program team was required to set aside capital in the event of a default. "I want to get program teams to say it's worth the investment. I want them to have 'skin in the game' and make trade-offs on how they use their budget dollars," Sunderland says.

WHITE KNIGHT

Peter Wagner was an internationally recognized scientist, not a businessman. He co-

was making enough forward progress that the HIV diagnostics team was optimistic that the company still had a chance to bring its CD4 test to market in the developing world.

Management of the Gates Foundation's investment fell to Yip as well as the experts on the HIV diagnostics team. Yip raised concerns about the company's financial struggles, but the team pushed back with the importance of Zyomyx's product.

Zyomyx's white knight appeared to arrive in the form of global pharmaceutical giant Mylan NV, a company with nearly \$8 billion in annual revenues globally. Mylan had first held discussions with Zyomyx in 2009 after Zyomyx's CD4 test demonstrated proof-of-concept. In 2012, after meeting again at a J.P. Morgan conference, the two firms began serious partnership discussions. Zyomyx's cash was running low. Mylan could be the global distribution partner that would finally propel the CD4 test to market.

"The technology was fantastic," says Anil Soni, Mylan's global leader for infectious diseases, who took the lead on the Zyomyx partnership. "Mylan strongly believes in the idea of doing good and doing well. While we always recognized that this wasn't going to be a blockbuster, we were willing to make the investment because we were looking at it from the perspective of enhancing pa-

tient access to treatment. We believed that an improved diagnostic closer to the point-of-care for HIV-positive patients could really advance the ability to get patients on treatment."

Leveraging its rights as a secured creditor to Zyomyx's intellectual property rights, the Gates Foundation insisted on extending its global access agreement to any deal with Mylan; should the test come to market by way of Mylan, it would remain accessible to the very poor. This agreement would limit the future price at which the Zyomyx test could be sold in countries with high rates of HIV.

Mylan's financial analysis was able to accommodate the price cap because, as a huge seller of generic antiretrovirals, the company didn't need to make money on the



Eric Tebove holds up his HIV negative test results after visiting a clinic on the outskirts of Lusaka, Zambia.

age to ensure that the company continued to pursue the charitable objective—getting an affordable HIV diagnostic test into rural clinics across sub-Saharan Africa.

The PRI team did the deal, but their financial analysis indicated little chance of repayment. Significant engagement would be required from the foundation's HIV diagnostics team to monitor the company's progress closely. The PRI program included a mechanism to allocate the investment funds, and any losses, between the PRI pool and the program team's budget.

The PRI team assigned the Zyomyx deal the maximum "Risk Share" rating—100 percent. That meant that the foundation's program investment officers were almost certain the investment would fail from a financial point of view, and therefore felt

founded Zyomyx in 1998 and became CEO in 2005, but his team had struggled to commercialize products. And he hadn't raised the capital needed to get the CD4 test into African health clinics.

"He was a great founder and extremely brilliant, but building a company was a new challenge," says Jenny Yip, a senior program investment officer who joined the Gates Foundation's PRI team in 2012 after 10 years as an investment banker at Goldman Sachs.

Even with the foundation's capital, Zyomyx struggled through a series of technical problems that delayed the product development timeline and caused the company to miss many of its milestones. Cost estimates climbed as the Zyomyx team worked through the technical difficulties. Yet the company

Zyomyx test. The company would benefit from point-of-care HIV diagnostics without the need to build out costly infrastructure by helping ensure more patients received access to its leading portfolio of HIV products. Already, approximately 50 percent of patients on antiretroviral therapy treatments around the world relied on a Mylan product. Mylan viewed the Zyomyx deal as an opportunity to further differentiate itself in this highly competitive space.

Zyomyx's technology continued to show progress and developing country demand was high. According to Soni, Wagner, Zyomyx's CEO, sold Mylan hard on the investors he had lined up should Mylan come on board. In June 2013, Mylan agreed to in-

interested never materialized, and Zyomyx raised no new money. Few investors would even consider a high-risk product solely aimed for the developing world, with requisite low prices and thin margins. In the midst of yet another cash crunch, Mylan provided more investment, this time a \$1.5 million loan. The risks were heightened when Zyomyx unexpectedly revised the costs of the manufacturing lines needed to produce at scale. Cost estimates nearly doubled from \$25 million to more than \$40 million.

Then the market shifted. Countries began to move away from using CD4 measurement to monitor drug treatment, in response to 2013 WHO guidelines that recommended they test viral load directly.

Even the [Gates] foundation's team of scientists and investment professionals couldn't rescue a struggling company in a difficult market.

vest \$6 million for a 20 percent equity stake in the company. In addition, for an exclusive distribution partnership, Mylan committed up to \$10 million in milestone payments over 10 years. Mylan saw the relatively small commitment as an opportunity to bring a game-changing product to market. The Gates Foundation capital and global health expertise made the deal easier.

The transaction triggered a partial conversion of the Gates Foundation loan to equity. Of the \$16 million total, the foundation converted \$9 million to equity, for a 48 percent stake in Zyomyx. Another \$760,000 went into Zyomyx's employee equity pool to help the company recruit and retain the talent needed to take its product across the finish line and reach people in need. The remaining \$7 million remained as senior secured debt, due in May 2023. As Zyomyx's largest equity holder and an observer on its board, the Gates Foundation had the tools to protect its charitable objectives.

COST TO MARKET

In spite of the financial rescue, it was not clear that Zyomyx had the wherewithal to bring the product to market. Almost immediately, Mylan saw warning signs. Zyomyx's December 2013 funding round was moved to January, then to the third quarter of 2014. The multiple investors who were said to be

Furthermore, it became clear that eventually the WHO would recommend treatment directly after diagnosis of the infection, eliminating the need for CD4 measurement altogether. The combination of increasing costs and declining public health impact made additional investment by both the Gates Foundation and Mylan unattractive.

"At the time, we made the argument that CD4 was still in use by millions of people, that Zyomyx's technology would still be beneficial," says Rousseau. "But in reality there's an opportunity cost. There were things we could now do that would have more impact."

Mylan's Soni downplays the impact of the market shift. "The testing was validating the product. The commercial market was smaller for sure, but there was still demand for product." For Mylan, what was untenable was the combination of Zyomyx's higher costs and failure to bring in any additional investment.

By June 2014, time was up. Zyomyx was burning through \$450,000 a month, costs were growing, and further delays loomed. After \$23 million in Gates Foundation funding (including the earlier grants), and more from Mylan, Zyomyx had no money in the bank.

Both the Gates Foundation and Mylan were losing faith. Even with low expectations, Mylan's return on investment looked

dismal, largely because of the higher than expected projected capital costs. In May 2014, Mylan decided it would not acquire the product or invest any further in Zyomyx.

The Gates Foundation also ruled out further financing. "This is a company and product that have consistently under-delivered and been significantly over budget for 3.5 years," wrote Andrew Farnum, who oversaw the investment for the PRI team, in a June 2014 email to Richard Henriques, the foundation's chief financial officer. (Farnum was recently named the foundation's new director of PRIs.)

To help the company wind down responsibly, the PRI team recommended one more \$356,000 bridge loan. That would let Zyomyx keep the lights on for two more weeks and give the program team time to decide on the project's future, as well as to document the technology in case it could be transferred to another developer in the future. The loan was made in July 2014. Zyomyx began to wind down a month later.

"We learned that no amount of even very advanced deal-making can offset an inherently flawed business model," says David Rossow, a senior program investment officer on the Gates Foundation's PRI team.

Innovation counts for little if the product or service never makes it to market. The foundation has engaged Intellectual Ventures' Global Good division to maintain the Zyomyx patents and find a commercial partner who will be able to use the Zyomyx intellectual property to bring the product to market. Probability of success is low.

"If we were presented with Zyomyx today, there's no way the foundation would do it," Yip says. "But it is by making mistakes like Zyomyx that we got to where we are today."

The outcome of the Gates Foundation's Zyomyx investment raises a simple question: if you're going to back an important project, why not bet on a more stable company? The answer is that innovation doesn't usually work that way. Large companies, like Mylan, can take an idea, commercialize it, and distribute it. But creating brilliant new technology, like Zyomyx's, entails risks that in most instances only a startup will take.

"Innovation happens at the startup level," says Yip. "But the idea is only 5 percent of the solution. Execution is the other 95 percent. We're shifting to a more balanced approach." ♦