



Your Money or Your Life

POZ asks Kevin Frost, CEO of the Foundation for AIDS Research, the \$100,000 question that HIV-positive inquiring minds want to know: Does it pay to cure AIDS?

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The Foundation for AIDS Research (amfAR) is one of the richest foundations in the world funding the hunt for the AIDS cure. Since 1985, it has invested nearly \$275 million in the development of basic science in private research labs hoping that with its financial backing, scientists will crack the code and shut down HIV for good. Kevin Frost, amfAR's CEO, goes where few others will—admitting that they are in red-hot pursuit of the holy grail: the end of AIDS.

In this climate of global economic instability, large pharmaceutical companies are increasingly beholden to their shareholders and, as a result, increasingly more risk-averse. As a result, the gap between biotech development—the spoils of indie labs—and the reality of those products being brought to market is widening dangerously. In a time when AIDS has topped all previous tallies for total number of deaths and the number of people living with—and orphaned by—the disease, there are inversely proportionate responses on the scientific and investment fronts.

Add to that mix the fact that, untreated, AIDS threatens to spread its deadly swath wider and exponentially faster than ever before. As a result, it will further undermine global economic stability by killing entire generations of workforces in developing nations, threatening to drain the federal reserves of nations around the world and leaving in its wake an uneducated army of abandoned children some 14 million-strong and growing daily.

This is the environment in which we are struggling to outwit one of the craftiest retroviruses known to man. Contrary to conspiracy theories and legitimate questions about certain parties' inherent interest in continuing the epidemic, Frost assures us that the world can no longer pay the price—both in terms of dollars and precious lives—of not putting an end to the AIDS pandemic.

Given the profitability of AIDS meds—the global market for antiretroviral therapy is expected to top \$10.6 billion by 2015—is it unreasonable to think that there is a financial disincentive to cure AIDS?

KF: Yes. The treatment model we've created is not economically sustainable. For every person we put on treatment, three more become infected. We're losing the numbers game in a very simple equation of one-against-three. There isn't enough money in the world to pay for the increasing costs associated with putting people on treatment and then maintaining that treatment over the

course of a lifetime. We can't treat our way out of this disease.

What happens when people switch off first-line treatments, which are often generic and therefore cheaper?

Most low- or middle-income countries could put people on treatment for about \$100 to \$150 [per person] a year. Places like Thailand and Brazil have made that commitment. Where you hit a barrier is the transition from first-line to second-line. Because even in the best-case scenario, second-line treatment generally will quadruple the cost. People fail first-line treatments in the developing world at about 20 percent to 30 percent over the course of two years. If 30 percent failed in the first two years, and you transitioned all of them to new drugs, the cost of that second-line program would be as expensive as the first-line program within two years because it's four times more expensive to put people on second-line treatment. Some countries will do their best to create second-line treatment models, but some are going to be faced with saying, "We made first-line available. We did the best we could. That's it."

How much does adherence, or lack of it, play into the failure of first-line therapies?

Not everything associated with the failure of these treatments is related to adherence, especially in the developing world. Other mitigating factors influence the efficacy of treatment regimens. Especially in low- and middle-income countries where people don't have access to clean water or nutrition, both of which affect [drug] absorption, [which in turns affects] therapeutic efficacy. We've got enormous challenges related to the sustainability of donor-influenced treatment regimens in the developing world. It's a race against time to find a durable solution before we see the collapse of these models.

Won't the President's Emergency Plan for AIDS Relief (PEPFAR) pay for treatment in the developing world?

Five or 10 years ago, people said we were never going to afford to treat people in Africa for HIV. But the Global Fund was created, and other organizations got involved, like the Clinton Foundation. Finally, along comes PEPFAR and says, "We're not going to let dollars be a reason that we can't do this." Now, large populations of people are being treated in Africa [and other countries]. Yet I don't think people understand how fragile that model is. And it's been made significantly more fragile by the meltdown on Wall Street.

PEPFAR was authorized at \$48 billion. If PEPFAR is appropriated at \$48 billion in the new Congress, I'll eat my shirt. Based on what the government had to do for Wall Street and Main Street, I don't think there's a snowball's chance in hell that we'll get \$48 billion for this program. We'll be lucky to get half that.

Where are your scientists looking the hardest? Better, cost-effective treatment or toward a vaccine?

AmfAR's focused on the cure. Other organizations are focused on vaccines. We continue to fund vaccine research. We continue to fund research on microbicides—we're particularly interested in rectal microbicides. But the truth is, we want to find a cure. There are two types of cures. There's a sterilizing cure, which rids the body of HIV. Everybody agrees with that definition. If you have HIV

on Monday and you don't on Tuesday, then you're cured. But there's another type of cure—a functional cure. Functional cure means that a person with HIV lives with it the rest of his or her life, but is largely unaffected by it or doesn't have any pathogenic state achieved by the presence of the virus.

With or without medication?

Some people might argue that if you can take a medication that functionally disables HIV, they might consider that a cure. I don't believe that lifelong treatment constitutes a cure. It constitutes a treatment for a state. A functional cure would be that HIV is present but is not causing pathology. There's a lot of creative gene therapy going on. We just did a think tank on a cure in Boston at MIT to explore the findings of the Berlin patient. He was HIV positive, had serious immune dysfunction and had been on antiretroviral therapy for a number of years. He was diagnosed with leukemia, and as a result of his leukemia needed to undergo a bone marrow transplant. In doing so, doctors in Berlin decided to look for a bone marrow match, a donor, who had the naturally occurring CCR5 delta 32 deletion [which prevents CD4s from becoming infected and destroyed by HIV]. They found that match, which is extraordinary. They did the bone marrow transplant and more than a year out have not been able to isolate HIV in this patient. He's not on treatment and has a fully functional immune system and no detectable HIV.

When the meeting started, we asked this room of scientists, "How many of you think that this patient has been functionally cured?" And the room I'd say was about half yes, half no. A day and a half later when the meeting was over, it was unanimous. Every scientist in the room believed that this patient had been cured.

But we're still a far cry from having a cure, right?

At the time the results of the Berlin case were published, Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health [NIH], said, "Look, bone marrow transplants are \$200,000. Who's going to pay for that?" That was entirely missing the point. The point wasn't that we can go around giving people bone marrow transplants; the point was whether or not we had a working hypothesis on which we could reverse-engineer some sort of solution to this problem. That's what amfAR is focused on—creative, innovative, cutting-edge ways of looking differently for a cure.

How long do you think it's going to take?

Anybody who's willing to make predictions about the pace of research is probably in the movie business. Research has this incredible capacity to surprise us. Sometimes it's not about just doing the experiment and finding the answer. Sometimes it's about doing the experiment and being surprised along the way.

We're not the NIH, and we don't have the money of a big pharmaceutical company. We're trying to light that flame that will lead to something that ultimately attracts pharma, and the NIH, to put the big money in and really make it something. Our job is to throw the pebble in the pond and watch for the ripples. That's how we characterize our research. That's why we're not afraid to talk about the cure. We're prepared to talk about the cure because ultimately that's where we're

going. To not talk about the cure is a lot more irresponsible than to talk about it.

So the investment of pharmaceutical companies is essential for bringing your research scientists' discoveries to market?

We would not have many of the treatments we have today were it not for the pharmaceutical companies. Pharma has a key role to play. Am I critical of pharma? Yes. There are a lot of things that I think pharma could do better than they're doing right now.

For example?

Well, too often the pharmaceutical approach has been "me too." If somebody comes up with a drug, for example, a nucleoside, then five other pharmaceutical companies come forward with nucleosides. Once it's proven to be a viable path everyone else gets on board. It's the smaller biotech companies that are likely to be more innovative in their approaches. I wish pharma was not so risk averse and they were more entrepreneurial in their research. But they are not. Pharma will tell you that basic science ain't their job. That's the NIH's job. Pharma sees their job as development.

The NIH says, "We don't make drugs, we just test them."

That's right. And to some extent, there's been some success in that model. AZT came out of the NIH and then it went into a pharmaceutical company. But if we rely solely on the NIH to explore the basic science and for pharmaceutical companies to develop the product, I don't think we're likely to see long-term success. Ultimately, the real answers aren't going to come from the NIH or pharma because they don't have the "Dream Team" mentality—they're not promoting the work of the best and the brightest.

Research scientists are not sitting in some lab thinking about where their next grant application is coming from; they're thinking, "Boy, wouldn't this be interesting." We've got to make more money available to younger scientists who are going to have the ideas that we haven't thought of yet.

The people who will have those ideas are scientists in their 20s, maybe 30s, who are just coming into the field. Our challenge is to figure out how to get them interested in HIV/AIDS research. How do we get them to apply new creative out-of-the-box thinking toward a solution to this problem? We do that through [programs like] our Mathilde Krim Fellowship program. The Institute of Medicine did a study about Nobel Prize winners. They asked, "At what age does the average Nobel Prize in medicine winner do their research?" The answer? On average, between the ages of 32 and 34. Today, on average, scientists get their first grant from the NIH at 43. NIH is funding people 10 years after they've done their most important work! That's not bringing young scientists into the system.

The truth is, pharmaceutical companies aren't looking for the cure. If there is a drug company looking for the cure, that's news to me. They do what they do best. Which is developing therapeutic treatments. They're looking for other people to establish the models—the proof of concept, if you will. Once the proof of concept has been established, then they'll figure out a way to market it and sell it.

And remember, simply developing a cure is not enough. You're gonna have to employ other players—including pharmaceutical companies—in order to deliver it. It's been said that if the cure for AIDS was a glass of water, we couldn't deliver it to a big part of the world. There are many parts of the world that don't have clean water. So it's not enough to just have the cure, we also need the infrastructure to deliver it.

What scientific developments look promising?

I see really interesting potential in gene therapy through CCR5. If we could down regulate CCR5 expression we might be able to create a functional cure. I was upset by the vaccine and microbicide setbacks. In a general sense the prevention field is a mess. However, we've got some very large PrEP [Pre-Exposure Prophylaxis] studies going on, and we might see the first results of those as early as summer of '09. And if PrEP works, that's a game changer. My theory is we're not really thinking of the ramifications of PrEP if it works. You're talking about giving a pill to people who are healthy, saying, "Here, take this for the rest of your life." Who is going to pay for that?

That doesn't really get us out of the problem that we're in right now.

PrEP has the potential to keep people safe, and it has scientific implications in terms of what it means to have a therapeutic treatment that prevents infection. It opens up whole new scientific avenues that can help us better understand infection and prevention. It will open up a new field of research. It's really going to change the face of the epidemic. But it's not going to change the economics. If anything, it's going to make the economics more challenging.

Is it realistic to think we'll find the cure to AIDS?

Sam Broder, who used to run the National Cancer Institute many years ago, said that research was like a flashlight—you shine it in the dark. And where you shine the flashlight suddenly becomes very clear. The problem is, you don't really know how big the dark is. All you know is what you're looking at. So research is like that flashlight. It illuminates something without really telling you how big the rest of it is. Are we closer, or farther? I have to believe we're closer. I have to believe there's reason to be optimistic through where the research is leading us. But how close? I'm prepared to be surprised.

What about the importance of the HIV community's activism? Would it help if the community were more engaged in advocating for a cure? Is it too quiet on the Western front?

It's always better when people are engaged. An informed consumer is always a better consumer. I wish we had a more robust advocacy environment in America today. Times have changed. On the other hand, in the developing world, advocacy is catching fire. It's extraordinary. You have the Treatment Action Campaign, groups in Uganda and in Asia like the Treatment Action Group in Thailand. These small advocacy groups are starting to come together in very impressive ways to take on the epidemic. Do I wish there were more engagement in the domestic epidemic? Yes. I really wish there were. But I think that in the developing world there's much to be enthusiastic about.

What's your vision of what will happen under the new administration?

Well, as we sit here at 5:30 on Tuesday afternoon, Election Day, without really knowing who the next administration is, my hope is that things will change for the better. People recognize that the President's Emergency Plan for AIDS Relief has been a very important program putting significant resources into fighting the epidemic globally. The call for a national AIDS strategy points out that domestically we need to do the same thing. We haven't risen to the challenge of the domestic AIDS epidemic; that was highlighted by the re-estimation of new infections by the CDC [Centers for Disease Control and Prevention]. When we have 50,000 to 60,000 people becoming newly infected every year, we're doing something wrong. We're not being honest about our desire to try and end the epidemic in America. My argument is, If you want to fight AIDS, for Christ's sake, take the gloves off! My hope is that this new administration will take the gloves off.

Won't the cure for AIDS make someone rich?

Whoever finds the cure for AIDS is going to make a fortune. To show you how much time has changed, consider this: The chairman of Merck was quoted in the 1950s in Time magazine as saying if Merck ever found the cure for cancer, they wouldn't patent it. Can you imagine somebody not patenting the cure for AIDS today?

I cannot!

I can't either. Does it pay to find a cure? Oh, you bet! They're gonna find a cure. And whoever finds it is going to make a lot of money from it—but, you know, as long as it's available to all who need it, God bless 'em.