



Drugs for the Masses

A new approach to developing and marketing a life-saving drug puts human welfare above mere profit.

The tiny protozoa, leishmania, introduced to the body via a sandfly bite, causes debilitating disease in 200 million people worldwide.

by ELLEN SCHWARTZ

REMEMBER THOSE choose-your-own-adventure stories that were popular in the 1980s? Often written as if the reader were the hero of the tale, the story led you, the protagonist, through one hair-raising adventure after another, until it left you in imminent danger of sure death, hanging by your fingernails from the edge of a sheer cliff. Then the story posed alternative plot developments. Do you fall to your death? Are you attacked by a ravenous tiger? Are you saved by a helicopter that swoops down and carries you away? You, the reader, make your choice, and then follow that plot thread into more adventures... until the next fork in the road.

This story – a story about science and business, about pharmaceutical sciences research and human rights – is like a choose-your-own-adventure. In this tale, UBC comes to a fork in the road. The university can pursue business as usual. Or it can choose the path of global citizenship.

The disease

Every good story has a back story. In this case, it's about science.

Leishmaniasis is a debilitating disease that afflicts some 200,000,000 people worldwide, mainly in India, Nepal, Bangladesh, Sudan and Brazil. Every year, 500,000 new cases occur.

The disease, caused by a parasite transmitted by the bite of a sandfly, is characterized by fever, anemia and weight loss and is fatal unless treated. It kills an estimated half-million people each year. Worse, it is spreading to new areas as populations migrate in response to conflicts, poverty and deforestation.

Leishmaniasis also has social and economic impacts. Because it often causes profound scarring of the skin and disfigurement, those affected suffer social isolation. Afflicted women, many of whom form the economic backbone of their communities, are unable to marry in many of the countries where the disease is endemic.

Immune suppression due to AIDS increases the risk of *leishmaniasis* by 10 to 100 times. Before highly active antiretroviral medications became widely available, *leishmaniasis* was the third most common parasitic infection in southern Europe.

Other debilitating afflictions common in third-world countries are caused by fungal infections, which can weaken and kill people who are weakened by other diseases or whose immune systems have been compromised. But people in all parts of the world are vulnerable to fatal fungal infections when their immune systems are compromised: cancer patients and AIDS sufferers, for example.

Fungal infections have become an issue in

North America, too. A form of *candidiasis* called *candidemia* is the fourth most common bloodstream infection among hospitalized patients in the US, especially low-birth-weight babies and surgical patients, occurring in eight of every 100,000 people per year. One study looked at 35,232 HIV-infected patients who attended outpatient clinics in 10 US cities between 1990 and 1998, and found that the incidence of *aspergillosis*, another fungal infection, was between five and 10 per 1,000.

The treatment

There is an available treatment common to *leishmaniasis* and fungal infections: Amphotericin B, developed 60 years ago. AmpB, as it is known, is highly effective, with cure rates of nearly 100 per cent. But AmpB has two serious limitations. It causes severe kidney toxicity, which means that it can be given only in small doses and for short periods. And it must be administered intravenously. This means that patients have to be hospitalized for four to five weeks while they are closely monitored, which in turn taxes health care systems that are already overburdened. The enormous challenges of cost, accessibility and storage, not to mention the possible side effect of infection that often results from IV treatment itself, mean that the effectiveness of AmpB is limited in the countries where it is needed most.

The professor

Enter Dr. Kishor Wasan, professor and chair of Pharmaceuticals and Biopharmaceutics, and a Distinguished University Scholar. His office in the Cunningham Building is cramped: bookshelves and filing cabinets overflow with texts, papers and journals, while various awards and plaques are tucked inconspicuously onto shelves and the corner of his desk.

But the laboratory next door, the Wasan Lab, is state-of-the-art, and this is where Wasan has been mounting a campaign against *leishmaniasis* and fungal infections for the past 13 years.

With the support of a grant from the Canadian Institutes of Health Research, and the collaboration of his wife, Dr. Ellen Wasan, a faculty member at BCIT, Wasan worked on developing a lipid formulation of AmpB, a formulation in which the drug molecules are suspended in a fatty solution. This version proved to be just as effective as the original

in reducing the amount of infection, and with greatly reduced renal side effects, since the lipids protect the body's organs from exposure to the medication. This allowed the dosage to be increased, from about 1 mg per kilogram of body weight to 5 mg per kilogram, which was a major breakthrough. But the lipid version still had to be administered intravenously, bringing with it the same problems of cost and accessibility, and putting it beyond the reach of most third-world countries.

So Wasan set out to develop an oral formulation of AmpB, one that would have the same effectiveness and reduced kidney toxicity of the intravenous lipid version.

The breakthrough

Back to the lab. Wasan was doing two studies, one using the intravenous lipid formulation of AmpB to fight fungal infections in animal models, and another working on oral lipid formulations of other drugs, to see how the lipids improved absorption of the drugs.

The two streams collided.

"We took the lipid experiments and combined them with AmpB for oral use," Wasan says. "Then we tested the resulting formulation on fungal infections in animals. We got results we couldn't believe. The oral version produced a significant decrease in fungal infection in rats, with no kidney toxicity."

With considerable excitement, Wasan took his discovery to Barbara Campbell, associate director of the University Industry Liaison Office (UILO), the agency that brings UBC discoveries to the private sector and arranges for licenses to develop them and bring them to market.

At this point, in true choose-your-own-adventure style, Dr. Wasan's discovery could have evolved in one of two directions: business as usual or business with a global human rights ethic.

Business as usual

We now pick up the other part of the story, the business saga.



Prof. Kishor Wasan heads the fight against leishmaniasis.

Traditionally, when a new drug or technology is discovered at UBC, the UILO looks for a partner who will advance the research and then commercialize and market the product. A portion of the revenue resulting from the license comes back to UBC and is shared with the original researcher.

Usually, the partner gets exclusive access to the property, which means that it is up to that company to determine how the product is marketed. Consider a new cancer drug, for example. Because it is extremely expensive to take a new drug through the clinical trials and regulatory approvals needed to bring it to market, the licensee could market the drug at a profit to countries in the developed world, earning back its investment and returning a profit to shareholders. UBC could suggest that the company make the drug available at cost to countries in the developing world. But that is at the company's discretion.

Some of UBC's past partnerships *have* incorporated humanitarian principles into the

business licenses. For example, UBC has been a leader in creating partnerships for bioactive compounds through the research of Dr. Ray Andersen. These partnerships return revenue from the commercialization of the therapeutic compounds to the country of origin for the benefit of the people and environment of the region. But in the past such provisions have been technology-specific, one-off instances, not the general rule.

Business the new way

“UBC did not have university-wide principles to guide the development of our commercial licenses from a global perspective,” Campbell says. “So we began the process of defining a set of principles that would ensure global access to UBC discoveries.”

The intellectual and social climate for such thinking was ideal. Martha Piper, during her years as president, defined the university’s role to “promote the values of a civil and sustainable society, and conduct outstanding research to serve the people of British Columbia, Canada, and the world.” Current president Stephen Toope fosters the idea of UBC as a global citizen, urging the development of university spin-offs not only for profit but also to benefit those in need around the world.

Activist students

Behind the scenes, another force has been at play. Universities Allied for Essential Medicines (UAEM) is an international student group that lobbies universities to fund research on “neglected diseases,” such as *leishmaniasis*, that don’t catch headlines but that affect millions of people around the world, mainly in poor countries. The organization also pushes universities to incorporate principles of global access to medicines into the commercial licenses they negotiate.

The UBC chapter of UAEM was, according to Barbara Campbell, instrumental in bringing the issue to Professor Toope’s attention, and, from there, to other administrative levels. “This raised awareness on campus and gave UILO the leverage we needed to advance the idea of global access as a university-wide principle.”

As a result, UBC has become the first university in Canada to put forward a broad strategy to provide global access to appropriate technologies, and these principles are now an

integral part of all of the university’s licensing decisions.

Global access

While these global access principles strive to ensure fair access to relevant technologies for the developing world, they still recognize the legitimate needs of industry licensees. For example, one of the principles says that UBC will endeavour to ensure that underprivileged populations have low-cost or at-cost access to our research innovations. Another states that the university will support environmentally friendly research and green alternatives, and will take the lead in community sustainability.

How will these principles be put into effect? The policy sets out a number of strategies, ranging from seeking partnerships with not-for-profit and charitable organizations, to provide funding for neglected disease areas, to negotiating licenses that ensure low-cost or at-cost access to technologies that have potential relevance to the developing world.

Developing AmpB

Back to Dr. Kishor Wasan and his discovery. Through UILO, UBC has partnered with iCo Therapeutics Inc., a Vancouver-based biotech company, to advance the development of AmpB. iCo is funding Wasan’s continuing research in the quest to develop an oral, effective, heat-stable and long-lasting formulation of AmpB.

It will take a great deal of work to get there. The next step is to conduct pre-clinical studies using the oral formulation in animal models, which will be conducted in the Wasan lab. Then further research and development will be needed to advance the drug through clinical trials on humans and on through regulatory approvals.

The next stage of research will benefit both the first-world and the third-world applications of the drug. At some point, though, the research will likely branch off in two directions: one formulation of AmpB targeted to the kinds of fungal infections associated with immune suppression, and another specifically designed to fight *leishmaniasis* and the virulent fungal infections prevalent in the third world. At that point, considerably more funding will be needed to develop the anti-*leishmaniasis* applications. That is where, Wasan hopes, a

charitable organization such as the Bill and Melinda Gates Foundation may step in. In the meantime, Campbell says, “UBC’s partnership with iCo ensures that its development of the formulation will embrace our global access objectives.”

Kishor Wasan is eager to take his research to the next level, and his team, including research associate Dr. Sheila Thornton, as well as a post-doctorate fellow and a research assistant, is already designing the next pre-clinical studies. Wasan is delighted with the synergy between science and business that has emerged in this case. “Three things came together: the medical need for the oral delivery of AmpB, our initial discovery, and the intellectual and social climate at UBC to support human rights and global access in the developing world.”

Financial Priorities

There’s no escaping the fact that UBC stands to make less money from a license that requires low-cost or at-cost access for poor populations than one that allows companies to develop, commercialize and market products entirely as they see fit. “Part of the global access approach is fair pricing, which could affect UBC’s return and the return to the researcher,” Campbell acknowledges. “But this is important to the university community. We want to see a societal impact for research that takes place at UBC in every instance where it matters to the third world.”

Kishor Wasan couldn’t agree more. “It would be lovely to make piles of money from my discovery,” he says. “But I don’t need it. I do fine. It’s a once-in-a-lifetime dream to be able to do this altruistic work.”

Wasan admits that, because of his family’s origins in India, he has a personal connection to the battle against *leishmaniasis*. Smiling wistfully, he says, “I would love to be there to see health care workers administer an oral dose of AmpB to an Indian child.”

Thanks to his own brilliant research, UBC’s commitment to global access and the support of a local biotech company in the further development of this life-saving drug, he may get his wish.

And the story looks to have a happy ending for millions of people around the world. ♦

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