Progress without profits?

A Bay Area firm's business model seeks to fill in the pharmaceutical industry's gaps.

BY DAVID FILMORE

To help build its own pipeline, San Francisco-based Institute for OneWorld Health has essentially tried to fashion itself as a recycling center for the drug discovery community. Instead of high-throughput assays, its screening efforts involve scouring industry and academia to locate what Ahvie Herskowitz, OneWorld Health's chief operating officer and chief medical officer, refers to as "low-hanging fruit." These are postdiscovery compounds that, having surfaced from abandoned projects or as unprofitable side notes to ongoing ones, already have substantial safety or efficacy data associated with them.

This strategy leaves free approximately $10 million of donated funds—up to now, mostly from the Bill & Melinda Gates Foundation—and 20 employees to tackle preclinical studies and clinical trials for only the most promising candidates to fight infectious disease in the developing world.

Finding these "under the radar screen" compounds, Herskowitz says, is part of what allows OneWorld Health to be what some might consider a contradiction in terms—a nonprofit pharmaceutical company.

There is a growing realization that nonprofit organizations and drug firms have potential synergies. For instance, in June the Biotechnology Industry Organization launched BIO Ventures for Global Health (*www.bvgh.org*), a nonprofit initiative designed to partner the biotechnology industry with donors and investors to target traditionally neglected diseases. Separately, companies such as GlaxoSmithKline and Chiron, as *Modern Drug Discovery* reported in September ("Tackling global diseases," p 23), are targeting vaccine projects to take advantage of an infrastructure and purchasing power largely supplied by the Gates Foundation and other groups.

What makes OneWorld somewhat unique, however, is that it combines the drug business and nonprofit motifs as the basis of a single organization.

Founded in 2000 by now CEO Victoria Hale, OneWorld aims to "fill in the gaps that exist in the regular pharmaceutical model," Herskowitz (who is Hale's husband) says. In addition to the recycling approach, the company's efforts may include other activities such as performing safety trials of antimalarial agents on underassessed populations like pregnant women or advancing a more sustainable biotechnology-based process, as opposed to a plant extraction, for producing established malaria drugs. Both of these are specific projects on OneWorld's wish list that are awaiting funding.

We "look very much like a pharmaceutical company," Herskowitz says. This, he explains, includes employing the same types of scientists with drug development and regulatory expertise, using the same "best practices," and taking similar opportunistic approaches to pursuing projects.

Although profit potential doesn't enter the equation, the economic feasibility of a project and likelihood of impacting the health of targeted populations guide the company's business decisions.

On the basis of her time as a scientist at Genentech and, prior to that, as an FDA reviewer, Herskowitz relates, Hale came to the conclusion in the mid-1990s that this approach was both possible and necessary "to meet markets that simply are not viable."

"The idea was best emphasized in the field of neglected infectious diseases," he says, "because, in essence, no new R&D had been done in those diseases for at least two to three decades."

Therapies for the parasitic illnesses Herskowitz refers to, including malaria, secretory diarrhea, Chagas' disease, and visceral leishmaniasis, today make up OneWorld's pipeline.

Paromomycin, the candidate for visceral leishmaniasis—also known as black fever, which kills about 200,000 people annually in Africa, Latin America, and the Indian subcontinent—is a good illustration of the low-hanging fruit strategy. The aminoglycoside was marketed in the West as a broad-spectrum antibiotic in the 1960s, and by the 1980s—through mergers and acquisitions—it ended up in the hands of Pharmacia & Upjohn. When sales were eclipsed by newer medicines, the drug firm donated the compound and the use of its data to the World Health Organization.

WHO's tropical disease research sponsored some early-stage trials for visceral leishmaniasis, but it ran out of funds for the project and shelved it. However, in 2002, after receiving a grant of more than $4 million from the Gates Foundation and assurances from the Indian government that it wanted to cooperate on getting an affordable drug

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OneWorld CEO Hale observed an opportunity and need for nonprofit drug development during time as an FDA reviewer and industry scientist.

approved, OneWorld Health decided to step in. By June 2003, OneWorld and WHO had initiated a 670-patient Phase III trial in Bihar, India, that is now in the final six-month follow-up stage. The company expects regulatory approval in India and either the United States or Europe in the first half of 2005.

"We knew it worked; there was a huge worldwide experience in terms of safety; and we had a large pharmaceutical company that had already gotten it approved in the United States years ago," Herskowitz recounts. All of this is allowing a quick and affordable charge to the finish line, he says.

OneWorld is now negotiating with local manufacturers in India, who will receive any revenue stream generated from drug sales to sustain production. In the end, the expected result is a 21-day regimen costing $10 or less—depending on market volume—that, trials have shown, permanently cures this otherwise rapidly fatal disease.

Not all compounds are going be this close to reaching market when OneWorld gets its hands on them, but the paromomycin project, Herskowitz stresses, is a good demonstration that this is a realistic model. Credibility will be a vital commodity in convincing the for-profit and academic worlds to hand over research to OneWorld. And that message already seems to be getting through.

OneWorld has gotten, Herskowitz says, about "200 unsolicited lists of opportunities from scientists in academia and industry for things we should be looking at." In addition, several intellectual property (IP) donations have been made.

Celera Genomics, for instance, contributed IP in 2001 that it didn't plan to use for a cysteine protease inhibitor called K-777. OneWorld is currently conducting preclinical studies on the compound to probe its potential for further development in Chagas' disease, a serious infection affecting 16–18 million Latin Americans.

More recently, in February, researchers from the University of California, Santa Barbara, donated patents for a novel application of calcium channel blockers—established cardiovascular medicines—for schistosomiasis, a parasitic flatworm that infects 200 million people worldwide.

"There are many dual-market drugs out there, not necessarily just for the developing world," Herskowitz says. Taking advantage of these opportunities to produce "win-win situations" for all parties involved, he adds, is a primary focus at OneWorld.

It is this type of thinking, for instance, that is driving "a beautiful separation of IP"—as Hale referred to it in her presentation at this year's BIO 2004 conference in June—between OneWorld and San Francisco-based Shaman Pharmaceuticals. Shaman is developing an intestinal chloride channel blocker for diarrhea and irritable bowel syndrome (IBS). Under terms of a deal currently being negotiated, Shaman is to retain rights to market all adult indications (e.g., traveler's and HIV-associated diarrhea, as well as IBS) and OneWorld can pursue development of a cure for pediatric secretory diarrhea, a leading killer of children under two years of age in the developing world.

Besides tax rebates and good publicity, Herskowitz says, Shaman will have access to any OneWorld results of overlapping significance, such as safety data, and will be paid for providing the active pharmaceutical ingredient.

One thing that OneWorld wants to avoid is becoming competition for firms and organizations trying to pursue global health projects. If activities in line with OneWorld's goals are being pursued somewhere else, it might take on a more traditional nonprofit role of financially supporting outside research, with the added bonus of providing expertise. It took this step in July, when it directed $1.4 million of Gates Foundation funding, along with a promise of regulatory consulting, to Sanaria, a Rockville, MD, biotechnology company working on a malaria vaccine.

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Or it might stay out of a field altogether, as it has with two giant scourges of the developing world, HIV and tuberculosis, which already have attracted substantial public–private partnership endeavors, Hale told her audience at BIO.

For now, OneWorld depends completely on philanthropy for its sustainability. This comes in the form of grants, IP donations, and volunteer scientists from industry and academia, which Hale, Herskowitz, and their team are trying to organize into a "pro bono" network. Clearly, OneWorld is anxious to get industry more involved in advancing global health goals by whatever model works

At BIO, Hale summarized some of the selling points for a for-profit company to target the developing world, including the opportunity of an open market with very little competition and partial subsidization by charity groups. But her bottom line was less straightforward material for a company's spreadsheet: "The value of innovation is measured not just by financial return but by the number of people you impact," she said. "The whole world is your market with infectious disease. [These diseases] are all going to move around the world eventually. We all know that. We just don't talk about it." ■

Institute for OneWorld Health pipeline

Project	Stage	Currently funded?
Visceral leishmaniasis		
Paromomycin	Phase III: Regulatory approval sought 2005	Yes
Chagas disease		
K777	Preclinical	Yes
Malaria		
Biotech-produced artemisinins	Preclinical	No
Malaria vaccine	Preclinical	Yes
Malaria drugs in pregnant patients	Portfolio screening	No
Diarrheal disease		
Adult drug	Phase II	No
Pediatric drug	Preclinical	No
Vaccine	Portfolio screening	No