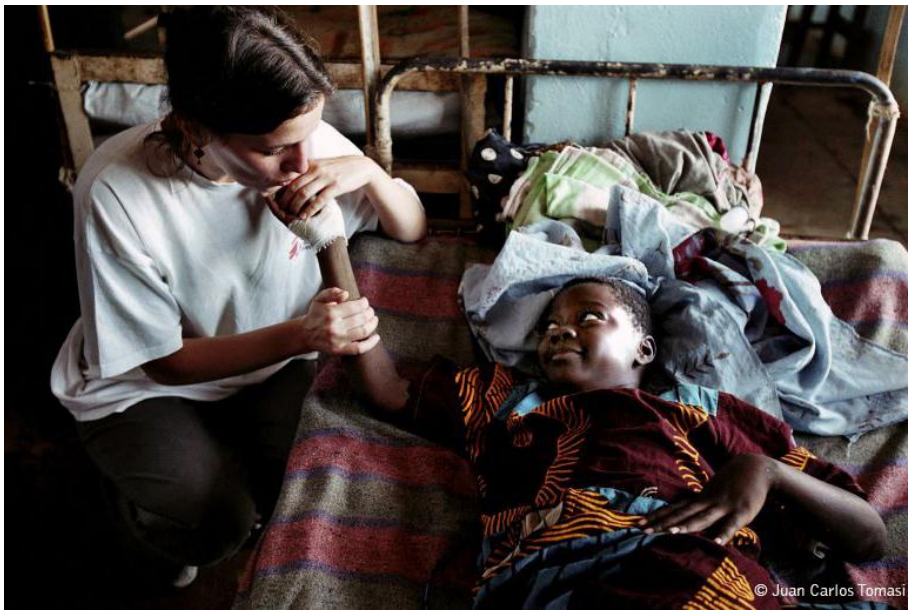
GLOBAL HEALTH
Innovation Insight Series



A patient with sleeping sickness is comforted by a caregiver from Medecins Sans Frontieres

ANACOR: Neglected Disease R&D Within a For-Profit Model

CALIFORNIA, USA

ESTABLISHED 2002

DAVID PERRY, CEO

THE PROBLEM/SOLUTION SPACE

Neglected diseases afflict the most impoverished populations in the world's poorest countries.[1] These bacterial and parasitic diseases thrive in remote rural areas, urban slums, and conflict zones where living conditions are substandard and access to healthcare is minimal.[2] Some neglected diseases such as hookworm, river blindness (onchoceriasis), and trachoma are chronic and/or disabling, leaving victims unable to work, attend school, or participate in family and community life. Others, such as malaria and leishmaniasis, are often fatal.

Although a staggering one out of six people suffer from neglected diseases globally, they lack visibility—and solutions—because these diseases disproportionately affect poor

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patients in low-resource environments in developing countries.[3] The need for vaccines, diagnostic tools, and therapeutics is urgent, but traditional business models of most for-profit biotechnology and pharmaceutical companies make it difficult for them to pursue solutions. New drug research and development is technically high-risk; only one out of every 250 candidate molecules that enters preclinical studies ever becomes an FDA-approved drug.[4] The process can also take a decade or longer, and is estimated to cost from $802 million to as much as $11 billion.[5,6] For companies that must answer to investors or shareholders, it is difficult to justify this vast expenditure of time and funds without a commercial market that offers significant returns.

Some large pharmaceutical companies are willing to devote funds to addressing global health issues in an effort to demonstrate corporate social responsibility and build public goodwill, but they generally require some financial risk-sharing from governments or nonprofits. Additionally, they are more likely to donate existing medicines and provide intellectual and financial capital than to initiate their own internal drug research and development (R&D) programs. Accordingly, early-stage R&D for neglected diseases often must come from the same small, entrepreneurial biotechnology companies that are driving a growing percent of drug innovation in the developed world.[7] However, although these small biotechs have the technology and expertise to pursue early stage R&D for neglected diseases, they lack the deep pockets and sustainable revenue streams to pursue unprofitable but humanitarian goals.

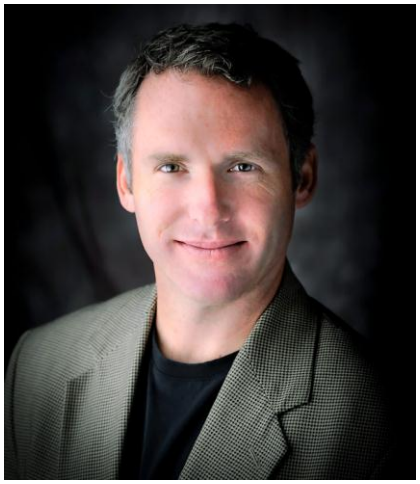


Photo courtesy of Eric Easom

Eric Easom leads Anacor's Neglected Diseases program

ABOUT ANACOR PHARMACEUTICALS, INC.

Anacor Pharmaceuticals, Inc. is a biotech firm founded in 2002 based on technology developed by Dr. Lucy Shapiro at Stanford University and Dr. Stephen Benkovic at Pennsylvania State University. The company focuses on discovering, developing, and commercializing novel small-molecule therapeutics derived from a unique boron chemistry platform. A for-profit company, Anacor went public in 2010.[8]

Boron-based compounds have a unique geometry, reactivity, and drug-like properties that enable them to interact with biological targets in novel ways, demonstrating the ability to solve important unmet needs for various diseases and conditions. Anacor's boron-based compounds have exhibited extensive preclinical and clinical activity in multiple disease areas, including fungal, inflammatory, and bacterial diseases (the company's core areas of focus), as well as in parasitic diseases. As of August 2012, Anacor had seven topical and systemic boron-based compounds in development, including tavaborole, a topical antifungal for the treatment of onychomycosis (fungal nail infection) and a topical anti-inflammatory for the treatment of atopic dermatitis and psoriasis.[9]

ONE CHALLENGE: NEGLECTED DISEASE R&D WITHIN A FOR-PROFIT MODEL

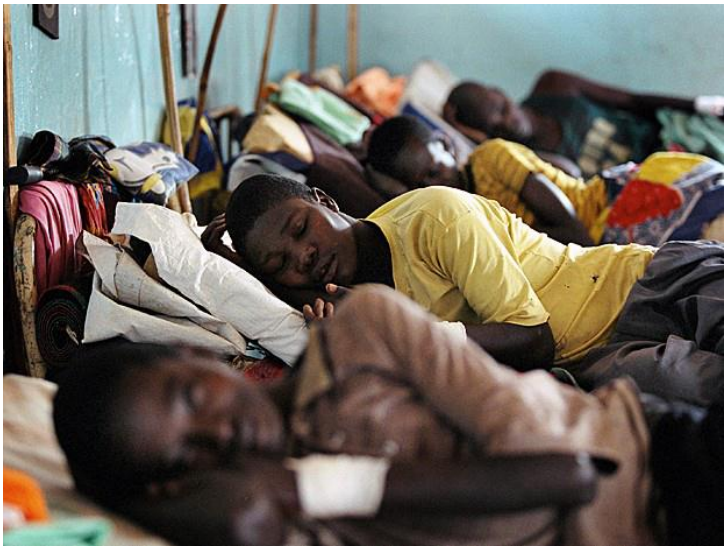
While performing early disease screening in the 2003-04 time frame, Anacor discovered that its boron chemistry platform showed activity against the causative agents of several neglected bacterial and parasitic diseases. Although CEO David Perry felt a responsibility to apply this technology to the neglected disease space, the company was venture-

backed and pre-revenue. As a result, devoting time and money to the pursuit of new therapies for complex, unprofitable global health markets would create a conflict with the objectives of its investors.

Despite these constraints, Perry was intrigued by the possibility of applying Anacor's platform to neglected diseases because he, like many others, perceived a need for real innovation in the global health space. As Eric Easom, a pharmaceutical industry veteran, described, "While repurposing existing drugs to benefit global health has and can provide incremental benefits, what was needed were breakthrough innovations—new products designed to address the significant unmet needs for specific neglected diseases."[10] The question facing Perry was how, as a small, for-profit biotech company, to realistically work on neglected diseases without compromising Anacor's obligations to its shareholders.

THE SOLUTION: DEFINING A CASH NEUTRAL R&D STRATEGY

Under Perry's leadership, Anacor took a preliminary first step into the global health field in late 2007 when it entered into an agreement with the nonprofit foundation DND*i* (Drugs for Neglected Diseases initiative). The company granted DND*i* a non-exclusive, royalty-free license to use its boron-based technologies to develop therapeutics for human trypanosome diseases—sleeping sickness, Chagas disease, and leishmaniasis. DND*i* was founded by Medicines Sans Frontiers (Doctors Without Borders) as a Product Development Partnership (PDP) to focus its drug development efforts primarily on neglected diseases, including the three trypanosome diseases.[11] Often designed as disease-based initiatives, PDPs brought together academics, large pharmaceutical companies, biotechnology companies with promising platforms for research and development, and funding from government and philanthropic sources to lead research and development efforts to address unmet medical needs. By creating a collaborative environment that included intellectual property and other information typically considered proprietary, PDPs fostered swifter, less costly development of global health technologies.[12]



A sleeping sickness ward in Tambura, Sudan

The PDP's early efforts showed particular promise with sleeping sickness, or Human African trypanosomiasis (HAT), which affected millions of people in 36 countries in sub-Saharan Africa.[13] Spread by the bite of an infected tsetse fly, HAT had two phases; a long first phase marked by intermittent fever, pain, and weakness as the organisms multiplied in the tissues, blood, and lymph; and a second, more acute phase in which the parasites invaded the central nervous system, causing mental deterioration, major sleep cycle disturbance, and coma. Without treatment, HAT was inevitably fatal.[14] Due to the toxicity of current drugs used to treat HAT (which caused death in approximately 5-10 percent of patients[15]), and because

some drugs were only effective in one phase of the disease, a spinal tap was used to confirm how far the disease had progressed before treatment was prescribed. Once decided upon, current treatments were administered via infusion, making them resource-intensive and difficult to provide in low-resource settings.[16]

As part of the HAT program, DND*i* engaged a contract research organization, Scynexis, Inc., to develop the early leads from Anacor into clinical drug candidates. Anacor served as a consultant and was reimbursed by DND*i* for expenses and fulltime employees dedicated to the project. Importantly, Anacor retained its IP rights for the compounds screened by Scynexis (outside the trypanosome areas and in some non-endemic geographies), as well as any new compounds that emerged from the partnership.[17]

Shortly after this initial agreement was put into place, Perry was introduced to Easom. Easom had become personally committed to global health after traveling to developing countries while working for a large pharmaceutical company. "I saw people who were sick, and learned that they were dying of diseases that didn't really have to be fatal. I decided that that was a good place to apply my skills for the rest of my career," he recounted. Perry and Easom engaged in a lively discussion about the possibility of applying Anacor's boron technologies to neglected diseases. Afterward, Easom went home and, over a single weekend, wrote a business plan that would allow Anacor to expand the applications of its technology to additional areas of significant need in the neglected diseases space.

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The plan, which Easom and Perry refined over the next several months, formalized Anacor's approach to using non-dilutive funding sources to underwrite this work. By leveraging foundation and government grants as well as PDP agreements to support its global health R&D efforts, Anacor could perform the work on a cash-neutral basis. "We felt like if we could do it by raising money, rather than spending shareholder money, then we should do it," said Easom, who became the company's Program Leader for Neglected Diseases.

In its next neglected disease partnerships, Easom modified Anacor's approach to position the company in a leadership role on these R&D programs. In these cases, the PDP compensated Anacor for the time its scientists dedicated to the projects. As of 2012, Anacor had agreements in place that enabled it to pursue treatments for malaria, onchoceriasis (river blindness), tuberculosis, animal African trypanosomiasis, cutaneous leishmaniasis, visceral leishmaniasis, Chagas disease, and shigellosis (bloody diarrhea).[18]

Despite some initial skepticism, Anacor's employees ultimately found working on neglected diseases motivating and compelling. As an unexpected benefit, the neglected disease work provided important funded research opportunities for Anacor's scientists, which was particularly valuable at points when the company's commercial projects transitioned into later stage development work performed by the clinical team.

Additionally, the pursuit of multiple diseases and programs fostered even broader exploration of Anacor's boron chemistry platform, enhancing the team's understanding and generating technology insights for future applications that could ultimately expand Anacor's commercial drug portfolio. "Working on neglected diseases has generated some serendipitous learning about our technology that, over the next few years, could generate important scientific breakthroughs," reported Easom.

Another benefit was the discovery of new, but related opportunities. For example, after several collaboration partners drew Anacor's attention to the significant overlap between neglected diseases and key animal health needs, the company decided to pursue the application of its technology to animal health markets. Anacor subsequently entered a collaborative agreement with Eli Lilly's ELANCO division to discover boron-based therapies for animal health uses. Under the terms of this deal, Anacor received an initial payment of $3.5 million, $6+ million in research funding, developmental and regulatory milestone-linked payments, and potential commercial royalties. Within a year of beginning the collaboration, ELANCO selected its first development compound arising from this collaboration.[19]

According to Easom, one more advantage to Anacor's involvement in global health was the positive publicity that raised the firm's profile and enhanced its reputation. "Anacor has become a leading company in this space," he said. "Hopefully, we are inspiring other small biotech companies to follow in our path to drive more much-needed innovation for neglected diseases." One 2012 industry report calculated that, so far, only 5 percent of all biotechnology companies were participating in neglected drug R&D.[20]

In terms of making this model work, Easom was quick to underscore the importance of fostering a company culture committed to supporting work in neglected diseases. In addition, he was adamant that the success of the program rested on leadership and commitment from the top. Perry offered unwavering support from the beginning, paving the way for Easom and the Anacor scientists to drive the program forward. "I am highly motivated to make working on neglected diseases sustainable, and ultimately beneficial for Anacor," summarized Easom. "It is my passion, but there is also that underlying understanding that I either have to make this work, or be out looking for a job. So I think that it's important to have somebody leading these efforts who is either extraordinarily passionate, or has a little bit of a 'do or die,' mentality. I have both."

By 2012, the HAT agreement had already demonstrated the promise of Anacor's global health R&D model. Through the collaboration, an Anacor compound was developed into the first new oral drug candidate specifically optimized to combat HAT. The drug entered Phase I clinical trials in March 2012.[21] "This drug will completely change the way HAT is treated," enthused Easom. "If this drug proves effective in both phases of HAT, you would have a safe and effective, simple-to-use oral medication. No longer would people have to rely on decades-old, toxic therapies that are difficult to use and require lumbar punctures to diagnose. This drug has the potential to lead to the eradication of this disease." Estimating that DND*i* spent roughly $10-15 million and just four years to develop the solution, Easom noted that this was "a good investment" in light of the vast potential benefits of the solution.

NOTES

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