Public-Private Partnerships in Drug Development for Underdeveloped Countries: An Interview with Craig Wheeler, President of Chiron's Biopharmaceutical Division

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In an effort to create a mechanism for addressing a critical need of providing medicines for economically developing countries, the Chiron Corporation and the Global Alliance for TB Drug Development have entered into an innovative public-private partnership. In the following interview, Craig Wheeler discusses the origins and nature of this agreement that could set a pattern for how corporations and nonprofit organizations can work together in drug development.

Thomasine Kushner: Would you begin with some background information as to how the arrangement came about between Chiron and the Global Alliance for TB Drug Development? What made GATB an attractive partner?

Craig Wheeler: Prior to coming to Chiron 8 months ago, I spent 14 years with The Boston Consulting Group (BCG). The agreement between Chiron and GATB was, in a way, bringing things full circle for me. As a senior partner at BCG, one of my activities was to put together a partnership with the Rockefeller Foundation in New York in which BCG donated part of our consulting services. Working with Tim Evans in Rockefeller's Health Equities Division, we provided assistance to The Medicines to Malaria Venture (MMV), which was one of the first public-private partnerships put together for drug development. There had been problems in setting up the MMV with the World Health Organization, and our role was to structure the business plan for that organization.

Subsequent to that project, a relationship grew between the Rockefeller Foundation and BCG where we went on to work collaboratively in helping to create entities like GATB. Ironically, I actually worked with the Rockefeller Foundation to put together the initial business plan for GATB. We worked together for close to 8 months on that project—beginning with an initial meeting in Cape Town, South Africa, where the idea germinated, through a process where we brought industry, public sector, and developing world representatives together to decide what might be done, all the way to the actual creation and launching of the entity in a meeting in Bangkok last year.

Following the birth of GATB, I moved on to do a number of other things in my consulting role with the Rockefeller Foundation, including helping them with microbicides and assisting in setting up a health surveillance network called In Depth, which is basically an epidemiological research engine indigenous to African countries.

In due course, I ended up interviewing and joining Chiron last summer. Shortly after my arrival, I encountered the fact that Chiron was in possession of an experimental compound, PA-824.

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I had been aware of PA-824 through some of the previous work I had done on GATB, and now I learned that Chiron had acquired the compound that was probably the most promising early stage tuberculosis compound in development. It has been 30 years since there has been a new anti-TB drug, and there is reason to hope that PA-824 could be a breakthrough. Although only in the laboratory stage, it had shown to be effective in fighting drug-resistant strains of tuberculosis in in vitro tests; and, if it proves powerful enough, PS-824 may shorten the average tuberculosis treatment time of 6–9 months, a critical feature in getting more people to complete the therapy.

TK: Did that acquisition occur when Chiron purchased Patho Genesis?

CQ: Yes. However, the compound was not actively being worked on when Chiron picked it up. Patho Genesis had decided, based on business reasons, that they could not afford to pursue it. The TB market was not large enough in dollar terms to warrant the costs of clinical development, and, basically, it had been shelved.

GATB had contacted Chiron and expressed interest in developing the drug, and when I arrived at Chiron there were ongoing discussions with GATB, as well as other companies, in terms of what should be done with PA-824. In the course of these discussions, we looked at what GATB was asking for and what we were trying to do.

Mindful of the aims and capabilities of our two organizations, we tried to structure a partnership with GATB that allowed the drug to be taken into an environment where it was feasible for it to be developed. This is the whole design of public-private partnerships: they can do things that industry just would not have any economic incentive to do.

Additionally, and this is where it gets interesting in terms of public health and ethics versus profits and bottom line, the partnership also creates a potential for one of those rare win/win situations. If the drug does succeed, it guarantees that the treatment will be available to the developing world, where TB kills 2 million people a year, with 8 million new TB cases being identified each year. The arrangement also ensures—although somewhat reduced—a reasonable profit to the pharmaceutical companies. That was the whole concept behind creating GATB and what it is now trying to do.

TK: I hear biotech industry executives talk about the quandary they face in knowing of very promising compounds that need development but, at the same time, not having the capacity to do anything about it because of the company's responsibility to its shareholders. Would you talk about how you view the horns of that dilemma and the possible role that public-private agreements, such as Chiron's with GATB, could play in responding to that challenge?

CW: That's the problem exactly. You cannot look at the industry and say that the executives do not understand these issues. They understand them very well. However, they find themselves in a box because they do not have the mechanisms that allow them to invest in those drugs. It really comes down to numbers. Today, the most recent estimates I have read say that it costs $800 million to develop a new drug. An executive would reasonably ask, "How can I possibly justify that kind of investment?" The only way it is going to make sense in terms of feasibility, if you are thinking about a disease like tuberculosis, is where the

cost has to be pennies per dose. An executive also looks at the probabilities game and says, "If I am back in the preclinical stage and my chances of success are one in a hundred, do I put my money here where I have no return?" You are in a box, seemingly with no way out.

That is the very real ethical dilemma companies are facing, and there needs to be some kind of mechanism by which they can "break the compromise," as I call it. That, in fact, is the whole idea behind public-private partnerships: they provide a means of breaking the compromise.

TK: More specifically, what do you mean by "breaking the compromise"?

CW: I'll give you the example of PA-824. In this case, you have a company that says, "I can't invest in this drug." Why? Given the facts of tuberculosis, it is not a nonexistent market in the developed world; it's just a small market. As an executive, I look at those facts and conclude, "Maybe that would be a $150 million a year market—if we had a drug for it. But, if we do develop a drug, political pressures will require us to find some way to let that drug be more broadly used." Realistically, that $150 million is depressed because there will be the possibility of parallel imports of very cheap drugs. There is no escaping the fact that the return looks terrible.

Now, if you take an entity such as GATB, which is funded by the Bill and Melinda Gates Foundation and the Rockefeller Foundation, you are looking at a very different picture. GATB is backed by real money, already close to $50 million, with the possibility of bringing in more. The strength of that support enabled us to form a unique partnership to tackle a medical crisis in a new way. We each had our needs: Chiron needed to find someone to take that job of development forward. GATB needed a promising compound they could develop. Our agreement on PA-824 answered both needs, and then it became a matter of working out the details.

Specifically, Chiron received a very small upfront payment from GATB, as opposed to the usual partnership arrangement when you have a large upfront payment. In exchange, GATB assumes the responsibility of the preclinical phase 1 and phase 2 work. Having no intent to become a drug development company, they will contract out the clinical work. Under the terms of the agreement, at the end of phase 2, Chiron gets to look at the results and, if they look positive, we get to take the rights back for the developed world, but only under the conditions that: (1) Chiron agrees that GATB has full rights to the developing world, to develop the drug at whatever price is necessary to get the drug into a therapy; and (2) Chiron is obligated to reimburse GATB for their costs of phases 1 and 2.

With this kind of arrangement, the numbers improve significantly. From the perspective of an executive, I calculate that there is probably about a 70% chance of being successful. Using the discount factor, even if the market is smaller, it is still a positive payback. So, I only have to put the money in after I have a much better sense that it is going to work. If all goes well, I will have a product I can actually do something with, even though the return is not going to be anything like as big as if I had done it myself.

All of this takes into consideration, of course, that currently the drug is only in preclinical development and it will be years before it goes to clinical trials. As happens all the time, the drug could fail at any stage.

On GATB's side, they have their money refunded and they have a com-

mercial partner to help them to share in the cost of developing the manufacturing processes and everything else. They also have full rights to what they need, which is a new drug that will be used for tuberculosis in the developing world at whatever it takes to get it into therapy—so it is a winning situation for both.

This was our initial concept when we put GATB together. We said, "There needs to be a way to be able to take the drug far enough along so that the disincentives disappear and the price that the pharmaceutical industry has to pay is still a return on their product, but it's a lower return on a higher probability." This is the only way investing makes sense.

TK: I remember a conversation with the Chiron founder, Ed Penhoet, in which we discussed the AIDS crisis in Africa and the criticisms being leveled at the biotech industry as to "Why aren't you doing something for these people?" Although strongly agreeing that there was indeed a responsibility to help, he also pointed out that it needed to be a shared responsibility, not solely on the shoulders of biotech companies. His question at that time was "Where's the government?"

CW: It's very interesting when you look at these public-private partnerships; there's very little government money in them.

TK: Why is that the case?

CW: First, because it is hard for the government to actually give money to ventures of this kind because governments give grants for specific programs. That is very good for research but very inefficient for developing drugs. In contrast, the GATB is set up to run like a public company. It has an independent board that carries full fiduciary responsibility. Members include health officials from the United States and South Africa, a past president of Medecins Sans Frontiers, and drug industry executives—who recently, by the way, elected Chiron CEO Sean Lance as Chair. This structure makes it possible to bypass much of the red tape that goes with federal support. The advantage here is that an entity like GATB takes private-sector types of principles and puts a social mission on the organization as opposed to a bottom-line mission.

The great strength of GATB is that it can rely on funds to support its projects. It has a positive balance sheet, like we would have as a corporation. Consequently, it can decide to spend, shift spending, or consolidate programs at will. In contrast, what you see in traditional governmental funding, particularly in the United States, are cases of programs being funded for multiple years and, unfortunately, because of the cumbersome structure, they continue sometimes long after they should have been killed.

From the work I did in microbicides, I became aware of another kind of inefficiency. There are approximately half a dozen different microbicide projects being funded through government grants—they are only marginally different and none of them is fully funded. The right thing to do, in my mind, is to pick the best one and put all the resources behind it. As it is, they are competing with each other for very limited resources. In the current context, this kind of shifting of funds is impossible. However, the reasoning behind establishing the GATB was to create a structure that moved away from funding models such as NIH and WHO and would work under its own board of directors.

TK: How did earlier attempts to establish public-private partnerships influence the development of GATB?

CW: In setting out to create GATB, we sat down with the Rockefeller Foundation and asked, "What would we do in a perfect world?" We decided that if it were possible to raise money, independent of other funding, the goal would be to create an independent partnership board guided by private-sector principles. And that is what we did.

TK: How do you see the future?

CW: GATB has got to prove to be successful. It exists at the nexus of *huge* pressures. There are a whole lot of people in the public sector who, although they will never say it, are waiting for it to fail and the chance to say, "I told you it was impossible to work with the private sector." Similarly, there is a great deal of suspicion in the private sector too, and so success is *critical*. Fortunately, GATB has a great CEO in Maria Freire, a former NIH Technology Transfer official.

TK: How important is a fuller public understanding of what is at stake?

CW: It is easy to be "armchair ethicists" without experiencing what the facts actually add up to in human lives. I remember attending a planning meeting in Ghana and being surrounded by children asking for money as we left our meeting site. One of the African delegates said to me, "I guess you know these children are all AIDS orphans." Suddenly, those children's faces took on an entirely new meaning. I also think about being in African villages where 70% of the adult population was infected. You walk away from those kinds of situations and say "How can you *not* think about these things?" Here in the developed world, most people are unaware of the real facts, and they buy into what I judge to be "incomplete arguments." I believe if we close ourselves off to the facts, either by choice or by ignorance, we are culpable for our moral failures. As a friend once commented as we talked about the problem of closed minds, "A mind is like a parachute; if it isn't open, it doesn't work." Our partnership with GATB is a way of opening minds to new models of possibilities and creating mechanisms to address needs that will dramatically improve global health and make a difference in people's lives.