

## Did George do the right thing?

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On July 2, at a private dining room in Rockefeller Center's Rainbow Room (New York), SmithKline Beecham (SB, King of Prussia, PA) and Human Genome Sciences (HGS, Rockville, MD) made an "important" announcement. HGS's chairman and CEO, William Haseltine, and SB's J. P. Garnier, chief operating officer and president of pharmaceuticals and consumer health, outlined deals that brought four other pharmaceutical companies into the genomics era. Between them, Schering Plough (Madison, NJ), Synthelabo (Paris, France), Merck KGaA (Darmstadt, Germany), and Takeda (Osaka, Japan) would pay up to \$170 million licensing fees and milestone payments jointly to SB and HGS in return for access to the SB-HGS genomic resources. But the effects of this six-way corporate deal go far beyond these short-term financial considerations. For SB, the deal demonstrates that molecular knowledge can be traded not just for money but for security as well.

The story really begins in May 1993, when SB's president of research, George Poste, announced that he was going to sink some \$125 million dollars into HGS—then an unproven start-up. Since that time, pundits have debated whether George did the right thing. That deal rested on a three-legged stool, with J. Craig Venter's not-for-profit The Institute of Genomic Research (TIGR, Rockville, MD) doing the sequencing, William Haseltine's HGS focusing on functional screening of the sequences, and SB providing the money in return for downstream commercialization rights from this combined effort.

Outside researchers who wanted access to this data were asked to sign agreements that let SB secure the right of first refusal for commercialization. Critics said that George and SB had misjudged the reaction of the scientific community in expecting that they would be willing to make this kind of trade. Many saw this as a modern-day Faustian dilemma with, depending on who you talked to, either George, Bill, or Craig playing the role of the fellow with the long tail. More than once, the ire that scientists felt toward this effort to commercialize data access spilled over at meetings where one of these principals was in attendance.

There were good guys in this morality play, too: Within months of the SB-HGS announcement, Merck (Whitehouse Station, NJ) announced that it would set up its own competing sequencing project. Not only did Merck claim it could do the job for much less money than SB—around \$10 million—but it also promised that it would make the DNA sequences freely available to anyone by plac-

ing them in sequence databases such as dbest and GenBank. As of the end of June 1996, Merck had lived up to its promise: It had processed some some 48,731 unique transcripts into the public domain. Again, depending on who you talk to, this does or does not compare favorably to the 90,000 or so transcripts TIGR-HGS-SB claim—SB's detractors say the larger number of sequences claimed result from the less rigorous weeding out of sequences from the same gene.

Disgruntled executives within SB viewed Merck's entry into the sequencing race as a "spoiler's" tactic: Since Merck had been caught offguard by the original TIGR-HGS-SB deal, they argued, it moved to dilute the collaboration's value by making the data publicly available. Merck's management has always vehemently denied this charge.

The Rainbow Room announcement now recasts this drama in an entirely different light. In a cleverly constructed revision of their original agreement, Garnier and Haseltine announced that SB and HGS have shifted their focus from recruiting individual researchers to their genomics program, and instead, were inviting a select group of pharmaceutical companies to become members of their club. In return for membership fees, the initiates get the privilege of competing with SB and HGS to develop new drugs from the SB-HGS shared information base over the next five years.

In effect, these new players get to run a flat-out foot race with SB and HGS to see who will be first to turn sequence information into new drugs. The first stage of the race attempts to supplant one of the biotechnology companies' traditional roles by focusing on the discovery of therapeutic proteins. "The first company to show biological relevance in an animal model wins," says Haseltine. But after a company lays claim to a protein, the second stage of the competition starts: an all out sprint to see which company comes up with a small molecule analog, agonist or antagonist to the protein first.

What does all this achieve? Well, there is the \$170 million that HGS-SB collect upfront. But more impressive, perhaps, is the sheer horsepower that could be brought to bear on the SB-HGS data: Together, the collaborators devote over \$2.6 billion dollars to R&D—more than 25% of the US National Institutes of Health's (Bethesda, MD) budget—and collectively employ more than 13,000 scientists.

Understandably, Haseltine is positively ecstatic at the possibilities the new collaborations offer HGS: The funding and international alliances could potentially vault the company out of SB's shadow and into a world-class play-

er status. "As a result of this deal, HGS will build the discovery, manufacturing and sales components to make it a fully integrated pharmaceutical company," says Haseltine. "This will make it one of the first companies to do this since the start of the biotechnology revolution."

But the big winner in this deal is SB: In addition to its share of the cash, SB somehow convinced its new partners to sign over partial marketing rights for any drug—whether protein or small molecule—brought to market through this collaboration. Biotechnology and pharmaceutical executives interviewed for this article were uniformly surprised that SB had been able to negotiate this aspect of the agreement. The general consensus is that this is really what makes this deal "important." Garnier agrees. "This agreement represents a new paradigm for pharmaceutical deal making where companies collaborate in precompetitive research," he says.

What SB has done effectively refutes the megamerger mentality by playing out its hand more like a biotechnology company. Megamergers, aimed at cutting out redundancy between companies as the means to improve the bottom line, often begin this process with the "top down" cutting out of duplication of effort between R&D departments. The danger is that they will become huge marketing shells that are dependent on licensing in new technologies from the outside.

But this new SB collaboration takes the opposite tack. It promotes competition between pharmaceutical companies precisely at the R&D level. Winning will come from "bottom up" scientific discovery and innovation. The SB strategy will succeed only if this competition between the pharmas spawns better products faster than the megacompanies can license in. For biotechnology, SB's strategy represents both a challenge and an opportunity: If SB and collaborators can out biotechnology biotechnology in the R&D of therapeutic proteins, the role of biotechnology companies will be forever changed. But in the heat of this race, the opportunities for biotechnology product licensing to SB's competitors should be great.

While many questions remain, what will all this mean for George? For example, will SB be tempted to play both sides of the fence by cutting its own R&D while its collaborators bring it products? "It was George Poste's vision three years ago to use genes for currency," says Garnier. "We plan to expand our R&D efforts as a result." So, will George get a larger budget? "George always gets a larger budget." For the time being, despite his critics, it looks like George did the right thing. //