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How will biotechnology fare in pharma's big plan?

Faster. Cheaper. Better. Chief executives of biotechnology companies—and those who want to be CEOs—have used these words as an incantation to sell their companies to potential investors throughout biotechnology's brief history. Initially, the spell did not bind large pharmaceutical companies: They wanted small molecules and were hard pressed to see how the tools of molecular biology could galvanize their drug development pipelines. But now, DNA sequencing—perhaps one of the oldest and most widely used of all those tools—has changed all that.

The prospect that the Human Genome Project will be realized in the next 6 years has revamped large pharmaceutical companies' visions of drug development and biotechnology's role in that process. To be sure, the restructuring and consolidation that the pharmaceutical industry is undergoing has helped redirect their ideas about biotechnology. But something else is going on. While the officers and management of very few biotechnology companies know how to use genomics to promote their own drug discovery processes, nearly every major pharmaceutical company does (see *Nature Biotechnology* 14:926, 1996). In the words of one biotechnology vice president of research, "Big pharma's top management gets it."

This month's *Nature Biotechnology* lays out one of big pharma's plans. Jürgen Drews, Hoffmann-La Roche's president of global research, outlines his company's view of drug development in the 21st century. Roche's strategy will sound disarmingly familiar to biotechnology executives everywhere: Develop better drugs faster and more cost effectively through innovation. And where will these new methods and new products come from? Roche plans to modify the tools that biotechnology has assembled over the past decade and transform them into "power tools" for small molecule drug development.

With companies like Roche committed to using biotechnology as the core of their R&D program, it is easy to predict that the biotechnology industry itself is on the verge of a radical reorganization: Start-up biotechnology business plans can now aim at bottlenecks in the pharmaceutical development process rather than attempt to target amorphous unmet medical needs.

Biotechnology companies on the partnering circuit were among the first to see what was going on in the pharmaceutical industry—and are now struggling to be part of its genomic vision. No matter what companies used to do in "biotechnology," it seems that they have undergone collective corporate psychoanalysis and have discovered that deep down they are all really "genomics" companies. Companies developing therapeutic monoclonal antibodies (Mabs) are now "functional genomics" companies—using Mabs to sort out the role of newly discovered genomics targets. Those built

around constructing combinatorial libraries are now genomics drug discovery companies. Reagent manufacturers are now genomics supply companies. Companies that can fit themselves into the nooks and crannies of genomic pharmaceutical development should do well, because doing so should free them from money-raising concerns and allow them to direct their energies toward creating and enhancing new technologies.

But what about large biotechnology companies with products already on the market? In one sense, this time around, the biotech-pharma roles have been reversed. In the face of pharmaceutical companies trumpeting genomics as the way to make drugs faster, cheaper, and better, biotechnology companies have, at best, seemed confused about how to use the tools of genomics. But this past month, Genetics Institute (GI) charted a course for biotechnology companies looking for a way to incorporate genomics into their R&D plans with the formation of a de facto consortium around a technology it calls "DiscoverEase" (see "GI's genomics bid for secreted proteins" in the business news analysis section). The consortium—whose current members are Genentech and Chiron—will use GI's patented technology for fishing secreted proteins out of the genome. It is perhaps significant that all three founding companies in the consortium have major financial ties to big pharma: GI with American Home Products, Genentech with Hoffmann-La Roche, and Chiron with Ciba.

While this consortium will focus on developing recombinant proteins as drugs, recent successes at Genentech and Johnson & Johnson in reducing to smaller analogs the Z-domain of protein A (*Nature Biotechnology* 14:806, 1996) and erythropoietin (*Nature Biotechnology* 14:1060, 1996) indicate that many (if not all) companies view macromolecules as simply prototype drugs, with the revenues they generate desirable but somewhat incidental: Recombinant molecules are and will continue to be important in sorting out disease pathways, they can be used to demonstrate that a particular intervention addresses a particular disease, and they can serve as templates for small molecule drugs.

Given these schema, what are biotechnology's prospects? Biotechnology is now poised to enter the mainstream of drug development. Becoming central to the pharmaceutical industry's core technologies should give biotechnology a broader base and should allow it to attract an even broader spectrum of talent. This may be particularly true in the relatively risk-averse countries of Europe. Moreover, much of the fear the public expresses about biotechnology stems from the fact that relatively few individuals have experienced health benefits from biotechnology-created drugs to date. When biotechnology is seen as an integral part of an enterprise that regularly delivers innovative medicines, much of that opposition may be overcome. ///