
A New Wave of Collaboration Among Biotech Companies

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Despite recent declines in the biotech stock index, the biotechnology industry as a whole is reasonably well capitalized and in good health. More biotechnology companies are profitable than ever before, and many have the financial reserves to make it through the next couple of years, even if the IPO market does not become more receptive to biotech offerings. To capitalize on this financial strength, biotech companies are collaborating more frequently with each other, and collaborating in new ways with the large pharmaceutical companies (Pharma).

Until relatively recently, more often than not biotech companies took a technology or product to an early stage of development, then licensed that technology or product to big Pharma and collected progress payments and, if the technology or product succeeded, royalties. Today, however, the goal of biotech companies is more often to take products to later stage development through true collaboration, rather than to realize value from licensing deals or a sale of the business.

To fully appreciate this on-going change within the biotechnology industry away from the swapping of manufacturing and commercialization rights for royalties and toward the swapping of a portion of the rights for help in bringing products to market, it is useful to take a look at:

1. Past and present financial strength and trends in the industry,
2. Roadblocks for growth in the industry,
3. Solutions to the roadblocks, *e.g.*, strategic alliances,
4. Examples of recent types of alliances, and
5. Factors to consider when contemplating an alliance.

Financial Strength and Trends in the Biotech Industry

The Economy

In 2000, biotech companies raised over \$35 billion from public and private offerings, with 90 companies raising close to \$8 billion through initial public offerings.¹ In 2001, biotech companies raised less than \$16 billion, and only five firms went public on US exchanges. Compared to 1998 and 1999, when less than a total of \$17 billion was raised by biotech companies, 2000 proved to be all the more extraordinary, and 2001, though tumultuous at times, was a solid year for the industry. This year has been a different story, and the public markets have not been welcoming to biotech stocks.

Last year ended with four intra-industry acquisitions totaling nearly \$20 billion in value (including the largest merger in biotechnology's history: Amgen's acquisition of Immunex), and consolidation in the industry is likely to continue, but the number of transactions in which biotech companies can use their stock as currency will likely slow until biotech stock prices rebound.

Investor Expectations

The focus of investors in biotechnology has tended to swing between the "technology" sector of the industry (companies working to create the platform on which to develop products) and the "product" sector of the industry (companies working to develop patient drugs). In the late 1990s and 2000, the pendulum swung to technology with investors seeing value in genomics tools, a sub-sector of the industry that outperformed the remainder of the biotech market by a significant margin. Today, investor focus seems to have returned to the model of patient drug development, which has consistently provided more sustainable financial returns than the "technology of the day"

Convergence of Biotech and Pharma

Big pharmaceutical companies have generally focused on basic chemistry approaches to product

development, while biotech companies have more often focused on emerging molecular biology/genetic engineering approaches. In recent years, this dichotomy has eroded and both biotech companies and Pharmas are exploring emerging gene-based approaches, with Pharmas entering the field in part through the acquisition of and collaboration with genomics companies. More significantly, Pharmas are beginning to set up their own genomics units and decentralize their research and development operations in an effort to emulate the perceived research prowess of biotech companies (e.g., Pfizer, Glaxo-SmithKline, and Johnson & Johnson are said to have reorganized research and development operations into smaller units that focus more exclusively on research).

Roadblocks to Growth

The drug development cost necessary to reach late stage product development is the most significant obstacle for biotech companies in their attempt to shift from platform companies to product companies. The US biotech industry spends \$14 billion annually on research and development. Yet, the cost to bring a product to market can exceed \$500 million. Furthermore, due to regulatory requirements, it takes about eight or nine years on average to take a drug from research to market. For every 5,000 to 10,000 compounds screened, about five drug candidates emerge to clinical testing. From there, 80 percent of drug candidates pass Phase I; 30 percent pass Phase II; and 80 percent pass Phase III, leaving one FDA-approved drug. Even roughly accurate predictions as to success cannot be made until Phase II is completed, by which time enormous amounts of capital have been expended. Though many of the big Pharma companies have the necessary diversity of underlying technology, infrastructure, industry relationships, and financial resources to complete the process, biotech companies generally do not. In fact, well over half of biotech drugs approved in 2000 and 2001 were co-developed or marketed with big Pharma.

The Solution for Biotechs: Strategic Alliances

To help overcome the obstacles to bringing products to market, and indeed to begin to compete with big Pharma, biotech companies generally look to mutually beneficial collaborations. In recent years, as biotech companies have generally benefited from a steady inflow of investor dollars, true collaborations, not just licensing or mergers

and acquisitions deals, are more the norm. Through these collaborations, biotech companies are increasing their available resources and tapping into financial development, manufacturing, marketing, and sales strengths of others and offering their research innovation in exchange. Thoughtful and properly structured collaborations can reduce costs, diversify product lines, accelerate product development, increase eventual market penetration and profits, and thus create long-term value for collaboration participants.

The number of biotech collaborations or strategic alliances has recently been growing at over 20 percent per year, although the number of new biotech companies may be growing about as fast. The total number of such alliances was 121 in 1986, and 712 in 1998. Biotech funding from alliances is estimated to exceed \$5 billion/year, and has been increasing by more than 40 percent annually in recent years.²

Even though the number of Biotech/Pharma alliances decreased in the past year, the value of those deals increased significantly. The new financial leverage available to more and more biotech companies has reduced the need of those biotech companies to partner drug candidates early in development, and instead puts those biotech companies in better bargaining position with big Pharma (who continue to look to biotech companies' research to maintain new product pipelines and sustain earnings growth expectations).

The progress of products in the pipeline has always been, and is even more so today, an important driver of deal valuations. Late stage products provide substantial leverage and bring significant premiums. During the years 1998 to 2000, the average value of Biotech/Pharma alliances for drugs in late-stage development was \$110 million, but only \$60 million for products in early stages. More and more, biotech companies have the money to push their products further down the development pipeline before looking for collaboration help from big Pharma, and thus can retain greater product rights, and the resulting opportunity to capture more of the value of the end product. An example is Aviron's license of intranasal influenza vaccine FluMist to Wyeth-Ayerst Laboratories. Aviron retained the right to manufacture the product and to co-promote the product in the United States.

In addition, the number of Biotech/Biotech alliances is increasing. As the biotech industry has in recent years (but not as much in 2002) benefited from relatively easy access to cash, Biotech/Biotech alliances, as opposed to Biotech/Pharma alliances, look more attractive: Successful mergers are more likely between companies with similar cultures and big Biotech companies can present a compelling business strategy based on a more "go it alone" approach. This trend is probably here to stay, but could suffer if the capital markets remain tight into 2003 for biotech companies generally

Examples of Recent Alliances

Biotech-Biotech

CuraGen/Abgenix—over five years, CuraGen will identify 250 antigens across all diseases as potential drug targets. Joint selection teams made up of representatives from both companies will then select the most promising targets and Abgenix will use its “XenoMouse” technology to develop therapeutic antibodies at these targets. The collaborative goal is to create 24 drugs, with each company individually owning and commercializing 12, and each company paying cross-royalties.

Maxygen/InterMune—A license and collaboration agreement in which InterMune will clinically develop next-generation interferon gamma product candidates created by Maxygen. InterMune is funding development in exchange for exclusive worldwide commercialization rights for all human therapeutic indications. Maxygen receives upfront license fees, full research funding, development and commercialization milestone payments, and royalties on product sales.

Biotech-Pharma

CuraGen/Bayer—Potentially a \$1.5 billion deal, this alliance could be the most valuable drug discovery and development alliance ever for a biotech company (The troubled \$2 billion Bristol-Meyers Squibb/ Imclone deal is far from certain and on at least one occasion BMS has threatened to walk away from it.) Up front, Bayer purchased \$85 million in CuraGen stock and committed \$39 million to develop CuraGen’s databases. In return, CuraGen is to identify 80 gene and protein targets for obesity and diabetes drugs. Bayer will then find drugs that work on those targets. The deal calls for joint clinical development of 12 drug candidates, a 56/44 split of up to \$1.34 billion in development costs, and profit sharing in the same proportion.

Millennium Pharmaceuticals/Abbott Laboratories—The collaboration is to identify drug targets for obesity and diabetes and to develop drugs. Abbott bought \$250 million in Millennium stock. Although Millennium is not to receive royalties, Abbott will share (on a 50/50 basis) all discovery development and commercialization costs.

Vertex Pharmaceuticals/Novartis—Potentially a \$800 million deal. Novartis will pay Vertex \$215 million over six years in exchange for eight protein kinase drug candidates. If it delivers, Vertex gets up to \$200 million in interest-free, forgivable loans, as well as royalties; clinical development milestone payments could bring the total up to \$800 million. Novartis receives worldwide development, manufacturing, and marketing rights to the eight candidates, while Vertex receives co-promotion rights in the United States and Europe.

Biotech-Universities

Prana Biotechnology/Massachusetts General Hospital—Prana is funding Alzheimer’s research in exchange for an exclusive license to the patent application for use of Pramipexole, used in treatment of Parkinson’s disease and cocaine withdrawal.

Cepheid/University of Pittsburgh—Three year collaboration, in which Pitt researchers will identify and evaluate new genetic markers for several cancers, including lung, breast, esophagus, oral, head and neck, and melanoma; Cepheid’s “Smart Cyler” will be used to validate these markers for detection of cancer in lymph nodes.

Factors to Consider When Contemplating Collaboration

Strategic alliances have the potential to be more advantageous to biotech companies than traditional licensing and merger and acquisitions deals, and as the above transactions demonstrate, more biotech companies are in a position to negotiate such deals successfully. Certainly sharing of profits can be much more lucrative than receiving licensing fees, and buying into the strengths of others without buying into their weaknesses is less costly and less risky than an all encompassing merger or acquisition.

Which type of alliance is best for a particular company depends, however, on many factors, such as needs of both parties, type of technology, stage of product development, size of target market, patent position, etc. Yet, as with licensing and mergers and acquisitions, the most important factors to consider are finding the right partner and having the patience to structure the right deal.

Finding the Right Partner

Corporate cultures must be compatible; partners must respect each other; and corporate objectives must have compatible (not necessarily common) goals. Partners must also understand each other’s needs as to funding, technology, product, research and development, manufacturing, marketing, and distribution.

Structuring the Right Deal

The company must determine the value of what it has to offer (intellectual property technology, or something else) and settle with its partners on acceptable terms as to:

- Economics: cost/profit splits, milestones, equity/debt investment, upfront payments, royalties/licensing fees
- Allocations of decisionmaking power
- Ownership of resultant intellectual property
- Maximum product and technology values
- Term and termination

- Dispute resolution system

Conclusion

Alex To, head of Biotechnology Research Group, Credit Suisse First Boston, recently concluded that “[t]he technology explosion in the post-genomic era is fundamentally changing the industry infrastructure. Instead of conglomerates that can do it all from genetic research to product marketing, the biotech industry is now a matrix of supply chain relationships

along the drug discovery process, with increasing reliance on technology alliances and partnerships.”³

If biotech companies can return within the next year to the public markets, and thereby continue the strong in-flow of pre-public funding, they will continue to be able to bargain from strength with other biotech companies and with Pharma to craft alliances that are generally more advantageous to biotech companies than the licensing and mergers and acquisitions transactions seen throughout much of the 90s.

1. Sources of data in this article (unless stated otherwise): Focus on Fundamentals: The Biotechnology Report, Ernst & Young (2001), and BioWorld Bio Technology State of the Industry Report (2002).
2. David Chao *et al.*, “A Strategic Framework for Partnering,” *Modem Drug Discovery*, October 2000.
3. Focus on Fundamentals: The Biotechnology Report, Ernst & Young (2001.)