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BioMarket Trends

Capitalizing on Novel Expression Systems Up-and-Coming Technologies Reportedly Make Products More Efficiently and to Higher Standards

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Over the past decade there has been growing criticism of biopharmaceutical companies as they struggle to increase drug output. A new report by BioPlan Associates, "Genetic Expression Systems: Current and Future Manufacturing Platforms," highlights the slow shift of these companies as some begin to take advantage of recent technology platform advances to boost production.

In the early 1990s, many larger companies publicly announced that they would launch two or three new molecular entities (NMEs) per year, but they were eventually forced to backtrack and admit that these targets were simply not achievable. In 2007, the global pharmaceutical industry was investing 70% more in R&D than it did ten years earlier, yet generating 30% fewer NMEs.

Many companies lack new technologies and methodologies in their R&D, as a result the industry has looked to biotechnology to reinvigorate drug development and provide recognizable medical advances. BioPlan analyses, however, show that, even in this area, a general reluctance to modernize is endangering the future of several companies and could shut them out of the rapidly growing biopharmaceutical market.

The number of biotech compounds has been increasing steadily over the last 20 years, but rather than just concentrating on absolute drug output, the emphasis must also be on the quality of the drugs being produced and the means used to manufacture them.

A 2006 industry-wide analysis of pipelines revealed that 50–90% of the projects in development in the leading therapeutic areas were considered to have a novel mode of action. In this regard, there is no denying the innovation that biotechnology has brought to drug development.

Since 2005, biotech drugs have represented 22% of the NME output of the industry, and now account for a quarter of total R&D investment. Current annual worldwide recombinant product sales are of the order of $70 billion. In 2007, biotech drug sales grew by 12.5%—twice as fast as the pharmaceutical market.

Improving Success Rate

To reduce the risk associated with drug development, companies have been analyzing the time, resources, expense, and expertise they can allocate. As a result, during the 1980s and 1990s, companies were able to improve their success rates for recombinant protein (rDNA) and monoclonal antibody (mAb) therapeutics. The Tufts Center for Drug Development (CSDD) found that the overall success rate for a 1990–1997 cohort of rDNA therapeutics entering clinical trials was 35% compared with only 26% for a 1980–1997 cohort.

Yet, despite these improvements, CSDD identified efficient manufacturing as one of the core areas to be addressed if further advances were to be made in biotech success rates.

BioPlan's analyses have shown that since the 1970s when genetic engineering was still in its infancy, there has been little basic change in the technologies used for commercial-scale

manufacture of biopharmaceutical products. Virtually all current products are being manufactured by the same old, familiar technologies—primarily using E.coli, CHO cells, and Saccharomyces cerevisiae as hosts. Therefore, while cutting edge can be used to describe the general approach to biopharmaceutical drug development, the same term can, by no means, be used to describe the approach to their manufacture.

Certainly, regulatory factors come into play, but this lack of progress is baffling. There have been genuine advances in terms of platform technologies that offer companies significant advantages. This includes vast improvements in product yield and improved product quality and lowered operating and infrastructure costs. Furthermore, in such a competitive field, these technologies can provide a route for innovators to make their products unique.

In fact, the industry has been trending toward engineering its proteins with a focus on improving not just yield but also quality and clinical performance. According to Patrick Lucy, global business development leader for Dowpharma's Pfenex business, "Expression system platforms today must have the depth and breadth to meet both production and clinical expectations."

Lucy anticipates an increase in prokaryotic expression platforms due to their short cycle time in the fermentor and ease of genetic manipulation. "We are seeing a steep increase in inquiries from pharmaceutical companies that are now evaluating expression systems that exhibit efficient expression. Some of these companies had previously been defaulting to older mammalian cell culture simply because they have investments in large-scale mammalian production facilities."

Lucy feels that the older technologies are simply not sustainable over time. "Nearly all of our clients are indicating that they are making these shifts as a result of the high cost of manufacturing a pipeline of new molecules using older technologies. These products could and should be made more efficiently and to higher clinical standards in newer expression systems."

And, it's not just microbial systems that are generating interest. "Over the past 12 months, we have seen interest in new biopharmaceutical mammalian expression systems grow rapidly," explained Andrew Sandford, vp at Selexis. "Already, we have more than doubled the number of companies who have begun to actively change the way they plan their early development and manufacturing strategy. Many are now finding that they are able to start process development four to six months earlier; perhaps 50% have developed cell lines achieving titers of greater than 1 gram per liter productivities in, as yet, un-optimized conditions."

Window of Opportunity Still Exists

Any company involved in the biopharmaceutical sector, regardless of size, may have much to gain by taking account of the technologies available now. As highlighted by the BioPlan report, a number of companies are attempting to get ahead of their rivals before the advantages of early technology adoption and licensing are lost. This includes major companies, with some having paid millions of dollars to acquire companies whose only or primary assets are new manufacturing platforms.

Other companies have been quietly but actively investigating, optioning, licensing in, and implementing the new technologies they have encountered. For example, in 2006 Merck and Co. spent close to $400 million to acquire GlycoFi.

Industry observers noted that GlycoFi's yeast-based, protein-optimization technology complemented Merck's own capabilities in yeast expression, and that this would benefit the production of the virus-like particles in Gardasil. The move was seen as strengthening Merck's hand in oncology, which has been declared as one of its nine priority-disease areas for the future.

Similarly, in 2007, Hoffman-La Roche paid $52.5 million to acquire Therapeutic Human Polyclonals (THP). With its long-standing interest in innovative antibody research, the

acquisition was seen as an ideal fit for Roche. The initial intent of the deal was to allow Roche to gain access to THP's transgenic, rabbit-based mammalian platform for the creation of both monoclonal and polyclonal human antibodies.

Outlook

For companies that have been struggling to develop R&D strategies that will sustain their growth in the long term, biopharmaceuticals offer a promising opportunity. However, success in the new era will depend on more than a traditional attitude to resolving R&D issues and must encompass the technologies used for commercial-scale manufacture of biopharmaceutical products.

As the market becomes increasingly competitive, those companies that take advantage of the new platform technologies available will secure their industry position in the future. In contrast, those that allow the window of opportunity to lapse will find themselves unable to recover.