

A rosy outlook for **outsourcing** biologics



With over 20 years of experience in the biopharmaceutical industry, **Robert J. Broeze's** expertise spans research, development, characterization, validation, testing and cGMP manufacture of biopharmaceutical products.

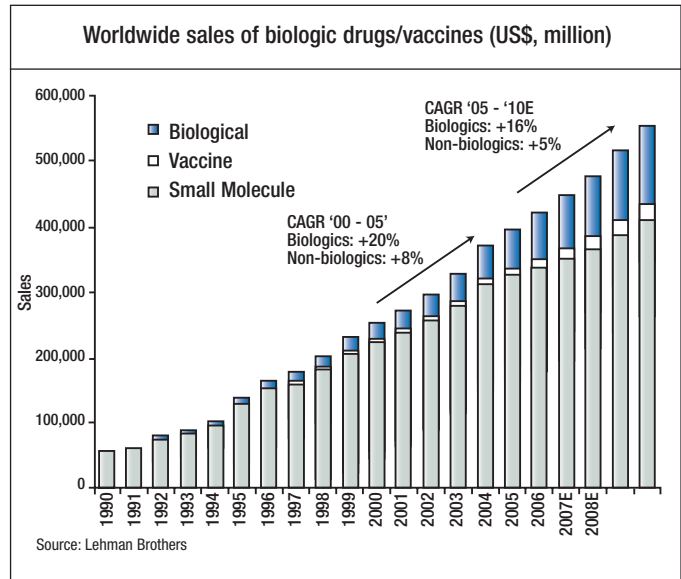
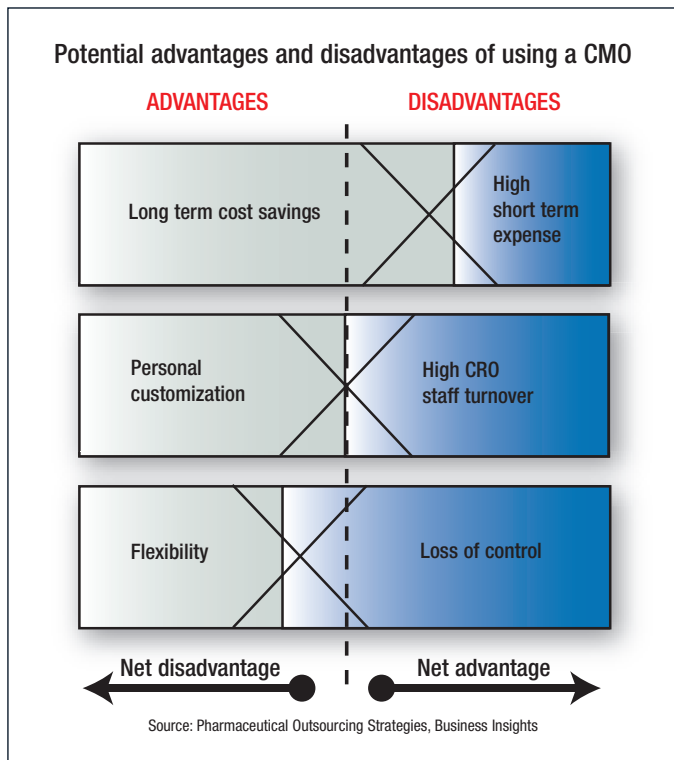
Outsourcing providers have every reason to be happy. With an increasing volume of new drugs entering the clinical trial pipeline, the usage occasions for contract services are up. *NGP* spoke with Laureate Pharma's **Robert Broeze** to find out how he plans to become 'most preferred CMO'.

Laureate Pharma can look forward to a future as impressive as its past. The contract manufacturing organization (CMO) achieved record growth in 2006. It signed 14 new agreements and increased its business backlog by more than 240 percent over 2005. "We also increased our company workforce by more than 25 percent to handle the ever-increasing workload. We are on track to completing the facility expansion, and have added a new pilot production plant to expand the purification production capacity," says Robert J. Broeze, President and CEO.

In June 2006, the CMO invested \$9 million to expand its manufacturing facility in Princeton.

The project, claims Broeze, is coming along great and the new pilot plant facility is already open for pre-clinical manufacturing. The new plant has two independent bioreactor and two purification suites, and has several stainless-steel stirred-tank bioreactors of up to 300L in size and disposable single-use bioreactors of up to 200L. Broeze: "We've installed filtration and chromatography skids for downstream purification of protein based molecules. The suites mimic GMP production facility and equipment and the projects can seamlessly transfer from pre-clinical development to GMP production."

Pilot plant services are done under non-GMP conditions, which saves clients more than two months of production time. "This is much desired by our clients, and we already have several customer projects lined up and scheduled to start now [March 2007]," says Broeze.



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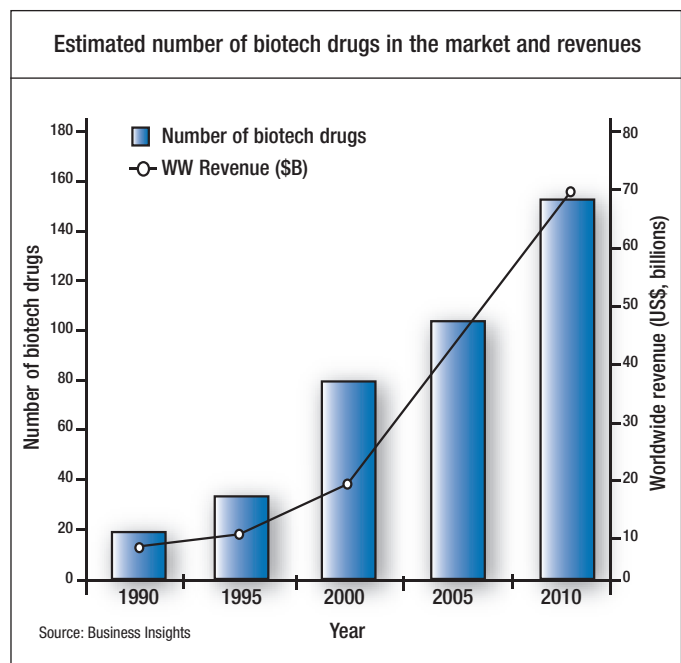
A growing market

The worldwide market for biotechnological drugs is estimated to reach almost \$70 billion by 2010. Analyses show an estimated compound growth rate of nearly 10 percent from 2005 to 2010^[4]. Sales from biologic drugs amounted to 11 percent of global sales in 2000. This climbed to 18 percent in 2005 and is expected to reach 26 percent by 2010.

Although the outlook is rosy, biologics manufacturing can be a risky endeavour. The process is technologically complex and highly regulated. Unlike the small molecules created by chemical synthesis, the large, complex protein structures produced in biologics manufacturing are instable and have a low tolerance for error. Even small temperature changes can have dramatic effects on the production process. Biologics manufacturing requires specialised capabilities, more planning, skilled staff and far more investment compared to small molecule manufacturing. As a result, striving for innovation and continuous improvement becomes ever more important in biopharmaceutical manufacturing.

“Evolving technologies continue to have a very positive impact on the industry,” agrees Broeze. His company uses disposable components and single-use bioreactor systems, which provide a number of quality, operational and economic advantages. Laureate also uses clean and pre-sterilized disposable components, thereby eliminating the need for cleaning and sterilization process steps. To add to this, the CMO employs single-use technologies extensively at various steps throughout its bioprocessing projects.

The list does not end there. “Quality is another area we focus on heavily for continuous improvement. And we are in the process of integrating lean manufacturing principles into our process. Our goal is to make Laureate the ‘most preferred CMO’ for biomanufacturing in the industry,” says Broeze. To support this, his company has formed a scientific advisory board comprised of well-respected industry leaders to help guide Laureate through its evaluation of new services and emerging technologies.



Laureate and Boehringer

Another strategy on Laureate’s way to ‘Most Preferred CMO’ is its key strategic alliance with Boehringer Ingelheim, which the two companies agreed last year. Broeze expects this collaboration to help especially those customers whose process has low yields and whose traditional cell line optimization techniques are not sufficient to increase yield rates.

“Access to Boehringer’s proprietary gene expression system, BI-HEX, and their development expertise will potentially increase yields, positively

impact overall manufacturing efficiency and reduce cost,” foresees Broeze. He expects that the alliance will also prove beneficial once early clinical phases are completed at Laureate.

“We will support modest phase III and commercial production requirements for indications where large-scale manufacturing is not needed. Where it is required for phase III and commercial product, access to Boehringer’s mammalian cell culture capacity of over 180,000L will be a major advantage.”

However, there are hurdles to be taken on the way to expanding Laureate’s service offerings. “We are beginning the process for exchanging information between our scientists,” says Broeze, whose aim is to develop a seamless transfer between the two companies. The biggest challenge, he admits, will be to fully understand and harmonize differences inherent in the existing equipment at both companies and develop concise and effective transfer methodologies.

To ensure a seamless transfer, Boehringer Ingelheim will provide Laureate with process for-

mats, which fit into Boehringer’s large-scale production facilities. “Compared to a non-customized process the client will save substantial time that is usually needed to adapt the process after it has been transferred to a different facility. A well-elaborated concept for the up and downstream development will support this,” explains Broeze.

For customers who choose to use the BI-HEX platform, cell line development, including clone development, will be performed at Boehringer Ingelheim. An early clone transfer, including the transfer of a media package to Laureate, is supposed to ensure the timely uptake of the project in order to start further process development. Process formats used for upstream as well as for downstream processing will fit both companies’ equipment.

Last but not least, early preparation for the manufacture of clinical phase III material at Boehringer Ingelheim will save additional time when the process is transferred back for late stage production. “It is a challenge,” Broeze concedes, “but we have thought it through and we are well on our way.”

The alliance will provide Laureate’s clients with a complete path from clinical-scale production at the CMO to large-scale commercial manufacturing at Boehringer Ingelheim. It shows that outsourcing will not only benefit small to medium biotechnology companies but also large pharmaceutical and biotech companies.

“There is a steady stream of biopharmaceutical products in clinical trials and approved biotechnology drugs are generating high levels of revenue. The market is growing for the foreseeable future at double-digit rates,” predicts Broeze. Laureate Pharma intend to make it to the top and have their strategies all planned out. “Adoption of single-use technologies in downstream processing and invention of more high expression cell lines will be the hottest areas of focus in the next few years. These two areas will have a profound positive influence on the biomanufacturing industry.” ■

REFERENCE TEXT

- [1] See Business Insights (2005)
[2] Lehman Brothers (2006)

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