Interview: Thomas FrÃ¼h â?? CEO, Bachem, Switzerland

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Advances in delivery technology and manufacturing costs have driven a surge of activity in peptide drug development, says Thomas FrÃ¼h, CEO of Bachem â?? the largest and most advanced peptide drug CMO in the world.

Peptide therapeutics are a hot topic in the pharma industry today â?? whatâ??s the story behind the emergence of this thriving niche?

Peptides are biologically active chemicals which have a variety of functions in our body. They have many advantages, mainly that they are highly active, very selective, and tend to have few side effects. There are disadvantages however, as they have relatively short half-lives, are usually not orally available as they are broken down in the digestive track, and relatively expensive to produce. In the past, these disadvantages were significant enough that big-pharma companies were not particularly interested in peptides, as they had more interesting opportunities to pursue.

However, over the last decade the pharma industry has been able to drastically reduce these disadvantages via the development of more sophisticated delivery systems such as encapsulation, implants, nasal sprays, and other delivery technologies. Meanwhile the peptide CMO industry, essentially Bachem and our three largest competitors, have been able to significantly increase production scale, improve efficiency and reduce unit cost by a significant margin. Together these factors have helped to make peptides much more interesting targets for pharmaceutical innovators, and this trend still continues strongly.

Where do you see the most dynamic clusters of activity around these molecules?

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There are many applications, but many are clustered around two key areas. The first is cancer, as lots of peptides are being used in cancer therapies and vaccines. More recently, we have seen a large number of peptides slated for the treatment of diabetes get approved. Many other peptides in this disease category are still in development.

To introduce Bachem, what is the role or position of the company in this dynamic peptide ecosystem?

We are a typical CMO focused 100 percent on peptides, and we are the clear leader in this field. Our slogan is â??Pioneering Partner for Peptidesâ?• and this says it all â?? we were the first CMO to bring peptide APIs to the market, and today represent the leading edge of technology in the field with the most advanced technological capabilities which allow us to synthesize the largest peptides economically. As a service provider and partner, we build close relationships and collaborations with our clients who are primarily pharmaceutical and biotech companies.

Today, we estimate that the market for peptide APIs is roughly USD 1.5 billion. Roughly 40% of this market is covered through in house manufacturing at pharma companies. About 35% is covered by the biggest four, of which Bachem is the largest. Then, there is a highly fragmented group of companies that for the most part lack critical mass. These companies command about 25% of the market. Bachem seeks to set the standard for the rest of the industry when it comes to quality of service, reliability, and capabilities.

As the leader in the peptide CMO industry, might Bachem look to grow via an M&A strategy?

Like other segments of the pharma industry, we face increasing regulatory requirements day by day as compliance requirements from the EMA and FDA are constantly increasing. Meeting these requirements requires that you have a strong quality assurance and compliance department, which means a certain number of employees in this field, and effectively this creates a minimum size requirement for manufacturers.

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Bachem has reached this size, but if we were larger it would reduce the relative burden of supporting such professionals, and allow us more room to make changes by allowing us to better absorb capital expenditure requirements. Smaller companies will struggle to meet the requirements of regulators when changes require them to make significant unplanned investments in equipment for instance, and as such I believe that there will be continued consolidation of the industry in the future.

We are interested in taking part in this consolidation, but this is not something you can plan. Thus, our strategy is to rely mostly on internal growth, but also keep an eye out for potential acquisitions which we will consider on a case by case basis. The peptide industry is small enough that there arenâ??t a large number of companies to consider acquiring.

One project which was announced was your partnership with Glytech to chemically synthesize Interferon Beta-1a. How disruptive was this accomplishment?

This project was really a demonstration of our capabilities to prepare the way for the future. Interferon is already on the market, produced by recombinant technologies, and as a chain of about 150 amino acids, itâ??s not really a peptide but rather a small protein with some glyco-chains. Our

intention was to show the pharma industry that as a peptide CMO we are capable of synthesizing molecules of this size and complexity economically so that in the future if they are developing a similar molecule they can consider having us synthesize it.

At present, the general rule is that big pharma outsources smaller peptides to the peptide CMOs, while the longer peptides are produced internally via recombinant technologies. Our goal is to push this dividing line further towards the â??long and complexâ?• end of the spectrum, and with this project we proved how far we could push synthetic capabilities at present. This is a great example of Bachemâ??s pioneering spirit, as just five years ago no-one would have been able to carry out such a synthesis at an industrial scale.

What are the advantages of producing a peptide synthetically versus using recombinant technology?

There are two or three major advantages. First, you can develop a synthetic process faster than a recombinant production platform. Second, the synthetic process is completely reproducible and the product is homogenous; with a biological cell line you can get biological impurities and heterogeneous expressions. Really, a chemical synthesis is much more controlled than biological cells can be.

However, as amino acid chains get longer the cost of synthesis eventually becomes too high, however we are trying to push this upward limit further. At present I think we could be competitive for molecules of a length around that of interferon, so around 150 amino acids. Something larger such as insulin we are still many years from being able to synthesize at industrial scale.

The way you serve your clients across this broad geography is quite complex â?? you could present how your different lines of business fit together and their importance to the business?

Bachem offers 360 degrees of service in peptides, and we are the only company to provide the full range. Starting in research we have a catalogue with more than 6000 amino acid derivatives, peptides and peptide fragments for use in R&D â?? these are used in drug discovery, as they can be used to inhibit or agonize a certain process so that researchers can try to modulate the effects with candidate molecules which they are screening. If they want a peptide which isnâ??t in our catalogue we can custom synthesize it. Our UK site is the center of excellence for such work.

Once our clients develop a target and begin pre-clinical testing they already need larger quantities for toxicity screening, metabolic testing, etc. This is when we transfer a project to either our Swiss or American facility and begin process optimization and scale up. Then we shift to the highly regulated cGMP world for clinical development, and scale up for our clients from phase I to phase III and eventually supply commercial quantities for the clients that market approved drugs.

Of course, along this path the vast majority of projects are dissolved, but for the one in ten or twenty projects that is successful, we have a variety of models under which we produce the product for the market. Under some circumstances we have exclusivity agreements, while after patent expiry, we can sell to the generic industry. Bachem has intense collaborations with leading generics players such as Sandoz and Teva.

On a revenue basis, about 20 percent of our revenues come from research peptides and pre-clinical supply. Of the remaining 80 percent, 60 percent of revenue is generated from marketed drugs, is for market supply while 40 percent covers clinical development. This is the natural equilibrium that has arisen, as our overall goal is to just keep the front end of our pipeline as wide as possible; we are able to adjust our capacity in time to meet expected demand, and thus we continuously monitor and

update our five-year plan to ensure we are ready for what we have in the pipeline.

To what extent do you try to select the best possible projects to collaborate on?

This is a subject we have regularly discussed, however our experience has thus far been that it is impossible to know which products will be successful in the end. Circumstances can change completely in a matter of days in this field, for example, when a young biotech with limited experience is acquired by a big pharma company. As such, we donâ??t filter the projects we take on as such, although there is a natural limit to what we can take on. Then, our lead times may increase and potential clients decide to work with our competitors instead. We are usually good at retaining the projects we deem most promising.

To illustrate, we have some projects which generate USD 100 to 200 thousand in sales per year, with others in the range of USD 10 to 15 million. One of the projects that is now generating USD 15 million per year was very difficult and risky in the beginning, the client was not easy to work with, and if we had been filtering projects based on our assessment of potential this one likely would have been refused.

What do our readers need to better understand about your business?

Our big pharma clients understand our business very well, as they have in-depth experience and know what we can do and how the development cycle works. They arenâ??t all easy to communicate with, but they understand how things work. The challenge can be with younger biotech companies that donâ??t always know precisely what they will need to file an IND application â?? thus they want to request all of the possible analytics and screenings possible to be sure they have the needed data to get the IND approval, yet they donâ??t have the cash. So the challenge is weighing what they need versus what they want, and both against what they can afford. Big pharma know what they need, and when they decide they need it they can afford speed and quality.

It can be very interesting to watch the transition when big pharma acquires a biotech. We might be working with one person at a biotech, moving conservatively and through phase I and early phase II â?? then big pharma swoops in and assigns a whole team of 50 people to develop the product. All have questions, suddenly they assign a huge list of requirements to be verified and analytics carried out, our internal team working on the project rapidly expands, and in a matter of days or weeks a project can go from one extreme to the other.

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