Fear Not, Peptides Are Here … To Stay

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In the pharmaceutical universe, peptides are in many ways a special case. They are synthesized chemically (about 90% of all peptide-based drugs[1]) but have many characteristics of biologic drugs (high specificity, low toxicity, complicated impurity profiles). Compared with biologics, peptides offer comparable patient benefits at a lower cost while generating higher revenues ($/g) than small molecules, making peptide-based drugs an interesting molecule class to develop and manufacture. Here is why:

Innovation Shows No Signs of Abating

Peptide drugs have been around since mid 1980s, when the first hormones opened the door for the whole drug class. Some thirty years later, the R&D pipeline of peptides is still strong. There are several hundred peptide-based drugs in the preclinical development. For the past few years, the pipeline showed double-digit growth which is expected to continue growing at the same pace. Peptide hormones are no longer the "hottest" class. Rather they gave way to venoms (like exenatide and eptifibatide) which were initially discovered in snakes and snails, but their synthetic versions found pharmacological applications in diabetes, stroke and pain.

Upcoming peptide drugs are targeting therapeutic areas of big unmet needs and high growth potential, such as oncology, infectious diseases, neurobiological disorders and obesity. Furthermore, peptides are components of vaccines (either as active ingredients or adjuvants) and can be used as targeting "devices" for other types of drugs or be conjugated to cytotoxics to make them more potent. The complexity of peptides, and hence manufacturing processes, is increasing. Consequently, more originators are choosing CMOs (custom manufacturing organizations) for peptide synthesis.

Complexity of peptide synthesis is driving CMO demand

Even though peptides are synthesized chemically, manufacturing peptides was never an easy task, particularly on the commercial scales. Big reactors are far from enough for the successful large-scale manufacturing. Limiting factors are more often large-scale handling of solvents, downstream processes and process development and scale-up. In the small-scale range, the synthesis is somewhat simpler and can be even automated by synthesizers. However, as soon as the process development for the scale-up is needed, most of the early originators will lack the know-how to take their products further through clinical development. In both cases, small and large scale, peptide CMOs with an extensive track record and proven expertise are in high demand. And they are only a handful.

As peptides are getting longer, often being cyclic, having unnatural amino acids and secondary modifications, the synthesis of peptides is more and more becoming an art. Innovation in manufacturing techniques (hybrid synthesis, chemical ligation, etc.) and process improvement are a must and increasing number of originators prefer to trust the peptide CMO experts. We expect that by 2012 as much as 50% of the total peptide API demand will be outsourced[2]. Partnering with a CMO, who is a true partner and not just mere supplier, that can handle the demand from development to off-patent supply, and has the right mix of innovation, experience, supply chain management and infrastructure can make all the difference. As the business models change from transactional to collaborational, both originators and CMOs will be heading towards an exciting and lively peptide future.

Asia is an opportunity rather than a threat

In the realm of small molecule manufacturing, manufacturers from China and India have taken over the highest market shares. Low cost base in these countries and increasing number of drugs turning generic, are both favorable for manufacturers from emerging countries, making the CMOs from higher cost developed countries uncompetitive. This is not the case for peptides CMOs. For small-scale non-GMP synthesis, there are indeed plenty CMOs in the market, mostly Chinese. Initially, their low cost production was in demand, but the unreliable and sometimes even questionable quality started to become a resistor, even at small scales. For large-scale GMP manufacture, there are almost no competitors from emerging markets. The reason is most probably the high barrier to entry built up of high volumes and prices of raw materials and solvents. Furthermore, regulatory requirements in terms of tolerated impurities are considerably higher for peptides than for small molecule drugs and meeting these demands is challenge, even for an established (western) CMO. At the same time, quite a few established peptide CMOs have or are setting up operations in India and China. As long as they leverage their experience, methodologies and quality scrutiny and profit from lower COGS Asian countries are famous for, their customers will generally be accepting.

Generic erosion is not particularly strong

Of about 50 marketed peptide drugs, two-thirds are already generic, and by 2014 several other peptide "blockbusters" will become generic (bivalirudin, pramlintide, exenatide). The impact of generic competition, however, will not be nearly as devastating as for the small molecule drugs. It is estimated that a generic peptide drug retains about 70% of its original price and about 80% of the drug volume is still manufactured by the originator or its preferred CMO. This is a consequence of the complicated manufacturing processes and large consumption of solvents and raw materials, which makes it difficult for generic manufacturers to be successful in this market. Interestingly, the top 3 selling peptide drugs in 2009, leuprorelin, octreotide and goserelin, are all generic and still generating billion dollar revenues[3]. Combined sales of those three products composed about 50% of the total $8.5 billion peptide drug market. Revenue growth of the peptide market is expected to continue at a rate of 7-8% p.a.;, which is quite impressive for a maturing market. So, what to expect from the future?

From 2011 beyond, the pharmaceutical industry will be bracing itself for the patent cliff impact and the hit is going to be significant. By 2014 drug originators are expected to lose $78 billion from patent expiries[4] (mostly from small molecule blockbusters) and biosimilars are posing a bigger and bigger threat to biologic drugs. But in the midst of this storm, all is well in the eyes of the peptide manufacturer.

[1] Tufts Institute
[2] Lonza Custom Manufacturing, Marketing & Intelligence
[3] IMS Health
[4] Datamonitor-Key Pharmaceutical Trends in 2010

Sanja Kais earned her PhD in molecular biology from the University of Zurich in 2008. For the past several years she has held different marketing roles for Lonza and is currently the lead for market intelligence for the peptide market.