Interview with Keith Martin, CEO, Apitope

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Tags: Apitope

Apitope’s research and success is based on its High Speed Technology Platform that uses soluble peptides as vehicles to regulate immune responses in patients. What is the history behind this technology and how does it differ from other peptide-based research?

Apitope was founded on a platform technology to discover peptides that we call apitopes, which is an acronym for Antigen Processing Independent Epitopes. Typically proteins will get broken down into small peptides that are presented on MHC II molecules to trigger immune responses. At Apitope we are developing these peptides to administer them to patients as injections or in other preparations in order to induce tolerance to the antigenic protein from which the peptide epitope was derived rather than driving the immune system to treat them as foreign proteins. This is based on the normal process by which the immune system becomes tolerant to its own proteins. One of the critical factors for success is to find peptides that will bind to the MHC II molecule in the correct conformation to induce tolerance to the protein rather than just the peptide itself. Our technology platform allows us to find these peptides that when injected will bind in the right conformation and will induce tolerance to the whole protein.

The distinguishing feature of Apitope’s approach is that we are using peptides that are more likely to function as tolerogens when used in the clinic as opposed to taking any peptide epitope and testing it by trial and error.

It is especially important to note that by inducing tolerance in this way we can be very selective in targeting the part of the immune system that is responding abnormally to a target antigen,

whether self or foreign. In doing this we are able to treat the underlying cause of the disease instead of only the symptoms. For example, our lead development program for multiple sclerosis (MS) is designed to prevent the immune system from attacking the nervous system. This can effectively stop the disease in its tracks. Rather than shutting down the entire immune system, our product candidate only targets the malfunctioning aspect of the system and is able to reset it to behave normally.
We have yet to complete our clinical program to make sure that the product truly works, but based on our pre-clinical data there is evidence that we are able to modify the progression of the disease with this approach.

Aside from the multiple sclerosis product candidates that Apitope is researching in partnership with Merck Serono, the company also has four other products that it is looking to develop. Is the idea to look for additional partners for the development of these products or will Apitope do this on its own?

Apitope’s strategy for our other product candidates is to take them from discovery up until Phase II clinical trials, at which point we would look to partner with another company that would have the capacity to take them forward into Phase III and eventual commercialization. Nevertheless, we are also flexible to partnering earlier than Phase II if an appropriate offer is made by a partner that we feel we could work well with us.

In terms of the kind of partnerships we are seeking, there are different ways in which this could happen. The first option is to partner on a R&D program that is already being developed by Apitope, such as the ones we currently have for Grave’s Disease and uveitis. Alternatively, we can also apply our technology to someone else’s preferred target disease or antigen in either allergy or autoimmune diseases. This kind of partnership would require us to start at the discovery phase by identifying epitopes that could treat a specific disease. From there we could either continue the research all the way through Phase II clinical trials or we could simply complete the discovery phase for our partner. Apitope’s team has a strong track record in taking Product Candidates from the bench to Phase II and we would encourage partners to take advantage of our expertise.

What other therapeutic areas could benefit from Apitope’s technology to develop innovative treatments?

Our technology can be used to treat any disease that is linked to a hypersensitivity of the immune system. This includes autoimmune diseases, such as MS, but it can also be used to treat more common afflictions such as allergies. At present, Apitope has decided to focus on autoimmune

diseases where there is a specialist hospital prescriber base. However, there are some allergies that are potentially life threatening and these would also represent interesting targets for us.

The other area of use for Apitope's technology is to treat intolerance to protein drugs, and this is illustrated by our third discovery program. with a serious potential problem for protein-based drugs is that after a year or two of treatment they can become inactivated by antibodies generated by the patient to the protein drug. One example of this is the treatment of haemophilia A with infusions of Factor VIII (a blood-clotting factor). Up to 30% of patients develop inactivating antibodies to Factor VIII. Apitope has a program that attempts to re-establish tolerance of these patient's immune systems to Factor VIII as not being a foreign protein and thereby allowing them to continue their treatment for haemophilia A with this therapy.

How would you assess the current opportunities for the biotech sector to partner with larger pharmaceutical companies?

We completed our deal with Merck Serono in early 2009, which means that we were negotiating this deal throughout the financial crisis of 2008. At that time we were also closing our financing from a number of sources. The environment is certainly difficult, but then it always has been. Biotech firms need to discover new products that address unmet needs and are clearly differentiated from products that are already available on the market or in development. Furthermore, there are greater expectations for biopharmaceutical products to bring something truly new, with improved efficacy and safety. Biotechs also have to deal with the important challenge of transmitting the message about their capabilities and technology to the key decision-makers in the industry and how this can add value to other companies. Apitope has been able to do this and continues to demonstrate large potential through its innovative technology, which explains why we have been able to attract investors and partners despite the difficult environment.

Ultimately, if you have good product candidates and a solid strategy to back up your research, then people should be interested to look into what you are doing and support it. Considering that our product candidates specifically target the underlying cause of a disease, and that we are also able to provide an improved side-effect profile due to the high level of specificity of our approach, we are confident that we will continue to build fruitful partnerships.

While even the most successful biotech companies are experiencing funding challenges with a 20% decrease in venture capital available for the sector, what other challenges has Apitope been experiencing on its path to success?

The main challenge we have had internally is to decide where we can make the most impact and demonstrate the value of the technology. This is particularly hard when you consider the wide spectrum of potential applications that Apitope's technology can be used for. Our decision to focus on Grave's Disease and uveitis was partly due to the fact that we should be able to obtain proof of principle in a clinical environment relatively early in the research program. While other diseases, such as Type I diabetes and rheumatoid arthritis, have huge markets, they also already have a reasonable number of therapies for their treatment. If we chose to target those diseases we would have to be able to demonstrate a step change in the treatment of these conditions when compared to those already on the market. Whilst we believe that our technology could certainly do this, given our limited resources as a small biotech, it makes more sense for us to focus on the areas where we can demonstrate the greatest impact. Ultimately we would like to find a partner that could fund the research for these more common diseases and take Apitope to the next stage of its development.

What makes you the partner of choice for such companies considering Apitope has not launched a single product into the market in almost 10 years?

First, it's not surprising that we have not had a produt launch since we started the company. Discovery and clinical trial generally take longer than 10 years to come to a product launch.

To begin with, we have a very innovative platform technology and a dedicated team that allows us to find peptides to treat serious autoimmune diseases and allergies. Second, the approach we are using has high probability of finding peptides with efficacy and an improved side-effect profile for those diseases.

Thirdly, we have managed to assemble an excellent team with a strong track record of taking products from the discovery phase through clinical trials and all the way to the market. This is definitely one of the key drivers of the company, because many biotechs find themselves in positions where they have great technology but they do not have the expertise to develop it commercially. Apitope's management team is outstanding in this regard and we are starting to see the benefits of it as we are driving our multiple programs forward very quickly.

After having worked for several multinational pharmaceutical companies, such as BASF and BTG, you endeavoured on your own venture with KetoCytonyx. After such rich experiences what was it that led you to head Apitope and what did you bring to the company?

One of the deciding factors to join Apitope was my belief that the company had a real opportunity to make a difference for the diseases it was working on. I had seen the pre-clinical data on the MS

program and saw its potential to become a disease modifier. Given the kinds of conditions faced by small biotech company, such an opportunity is critical to the ensure success. Being able to produce a therapy that will modify the course of the disease will make a huge difference in patient's lives particularly if this can be achieved without the side effects that come with other treatments. Essentially, I recognised a significant difference and opportunity in Apitope's technology.

Additional to that, Apitope has a solid scientific base with its founder, Prof David Wraith, being a renowned immunologist with a very strong track record in the field. The company had also received the necessary funding from investors, so I saw the opportunity to take all of this forward into the clinic with the company's first clinical trial. That trial subsequently led to our Series A funding in 2008 along with other of the company's milestones.

Even though Apitope's headquarters are based in Belgium, most of the company's research is based here in the UK. What are some of the advantages that the UK biotech sector offers companies such as Apitope?

In order to deliver on our key objectives in our MS program with our partner, we initially built a solid base in Bristol. Since then we have been expanding our operation in Belgium so that we have a strong foothold in both countries and can capitalise on the wide array of talent and expertise in both territiories. My comments here apply equally to both the UK and Belgium.

However, since your question is about the UK in particular, one of the main assets for biotech in the UK is the amount of people that have worked in big pharma and understand how to develop drugs. Not only do these people understand what needs to be done, but they are also deeply committed to bringing innovative products into the market.

Additional to this, the UK has some of the world's best universities that produce first-class scientific minds and where innovative research is being conducted. There are also some very good contract research organizations in the UK, both for pre-clinical and clinical research. For biotech companies such as Apitope, these CROs are very important because we conduct the discovery phase in-house and then do our clinical studies by out-sourcing the day to day activities to these organizations whilst retaining our close management oversight.

Thinking about the future, what are your personal ambitions for Apitope in five year's time?

First of all, I would like to see our lead program for MS successfully complete the clinical trial that it is currently on-going. After that, I expect to bring our new programs into the clinic to demonstrate that the platform is not only able to discover peptides, but we can also repeat our past successes

by taking them to the point that they reach the clinic and beyond. The last thing I would like to accomplish is to bring in more money for the company. This could either happen through another venture capital round or through a key partnership with a pharmaceutical company.

Does this also mean that you are considering to sell the company after you have reached certain milestones?

The reality is that all venture capital-backed companies are looking for an exit strategy for their shareholders and there are only two available options: an IPO or a trade sell. A trade sale represents a real exit for investors, whereas the IPO is in reality further fundraising. At the moment we are concentrating on building a viable business and attracting further financing, but at the same time we also have to consider what would make us attractive to provide an exit for our shareholders.

What is your final message for the readers of Pharmaceutical Executive?

We have built a solid company in the UK and we are now expanding it in Belgium. Throughout this process we have always kept in mind that the biotech and pharmaceutical industries are global businesses. This is why we define ourselves as a European biotech company rather than a British or Belgian one. It is also important to recognize that Apitope has very strong science as its base and a solid management team to drive this forward. Out of all of this we are expecting numerous successes in the near future and expect to see our product candidates commercialized into marketed therapies.

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