

Interview with Charles Woler, CEO, Endotis Pharma



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Endotis was incorporated in 2003 on the basis of a technology transfer from on a French public research institution. Can you elaborate on the origins?

The group was founded from near scratch in 2003 based on a specific project that was unsuccessful at the time but rejuvenated in 2005 with a focus on two major therapeutic areas: coagulation thrombosis and oncology. I joined the group two years ago to take care of the operations at the request of the investors.

At that time, we negotiated with Organon (now Merck) to in-license two innovative parenteral anti-coagulant compounds that were early stage and have since developed them to first human administration for one of them and ready to go in Phase 1 for the other one. Concurrent with these operations we synthesized our own patented molecule for coagulation but aiming oral administration (oligosaccharides are not orally bioavailable). The key characteristic for many of our compounds is that they're neutralizable thanks to avidin which is their specific antidote (developed in cooperation with Sigma tau which uses it for a different purpose. This represents a new paradigm because it allows you to clean the blood stream from one antidotable anticoagulant in a few minutes. It's a brand new principal to which Maurice Petitou who heads Endotis research contributed a great deal. Moreover, thanks to these oligosaccharides the world moved from extracted heparin to a synthetic compound which eradicates the contamination issues that can be typically associated with heparin, let alone pig shortage from which heparin is extracted. By matching these two advances we have created new value in this arena.

Endotis' other platform is in oncology where we are applying our knowledge small glycol drugs to create oncological compounds. From this research we have proven SGD have anti tumor activities

and we are close to drug candidates worthwhile pushing into pre-clinical development as well as proven that small glycol drugs can mobilize human stem-cells, which is thrilling data.

As you can see we have moved from an early stage research outfit to a company with a combined portfolio of advanced clinical and early stage compounds in two different therapeutic areas.

With a relatively short lifespan of the company how have you managed to be as successful as you have been in developing its current pipeline?

Everything is relative in life. What we all strive to do is license so-called relatively de-risked compounds which is what we did initially with our Organon licensing agreement. When you research anti-coagulant compounds like these there is already a proven function in humans so at the end of phase 1 you “only” have to find the right dose or doses for your phase 3 pivotal trials. What you do have to prove is safety being short or medium term and improvement on previous compounds. Therefore at the end of Phase I (with the exception of the dose) it’s as if you were at the end of Phase II with other compounds in new therapeutic areas.

Our oncology platform is clearly more risky than our thrombosis side because it involves trying new compounds. This allows you to raise capital on the relatively de-risked platform while also accessing government grants and incentive programs.

On the topic of financing, many biotechnology companies in France work in partnership with research institutes as a way of increasing knowledge and fiscal capital. What is your take on this strategy?

I am a member of the investment committee for the technology initiative of the INSERM. In my previous role I created and financed another start-up biotechnology company we got little public financing and engaged in several public-private partnerships. However, this is complicated and time consuming when it comes to pulling value out of public institutes in France. You can spend months in back and forth discussions and you have to find the appropriate balance with these interactions and also weigh the cost of not participating in them as well. I will say that if you do engage in these collaborations you have to do it for the right purpose: not just for the money.

In many markets, biotechnology companies note the risk of going public and losing control of the company. Nevertheless, from your previous experience that doesn’t appear to be a fear of yours. As the market begins to improve from the last two years, is an IPO something Endotis is considering?

While the market is getting better there are still not a lot of IPOs and I don’t believe the threshold has been met yet. All biotechnology companies are looking for one of several exits including an IPO, asset sale or an outright acquisition.

The profile of companies that would be appropriate for an IPO is changing as well. Savvy investors have noticed larger pharmaceutical companies currently require advanced compounds tailored to their strategy. In order to IPO on today's market you really need to meet niche requirements. Even if the IPO window reopens it will be different than what was seen over two years ago so I'm not sure if Endotis would be ready to make this move even if the market was different tomorrow.

At the moment we have about two years of cash available which puts us in a comfortable position; there is no need to sell off our assets in a rush. Timing, not just time, is of the essence.

In January, Endotis was invited to San Francisco for a JP Morgan health conference as one of the few private companies present. Did it take anyone by surprise to see an independent, French, biotech company there?

You're right to note that there are not that many French biotechnology companies that were also fewer private ones presenting at JP Morgan. Why us? I cannot say; you will have to ask them.

My personal interpretation is that Endotis doesn't tell a typical biotech story. Today, people are looking for compounds and whether or not you can find your place within the market. When you look at coagulation thrombosis it's a huge market so if you mimic what big pharma is doing then you can forget about competing. You have to find a different approach in a niche that could become over time significantly larger. For example with one of our injectable, antidotable compounds there are only one other solution: heparin and protamine. This combination is complicated to use while we offer a new product with a long half-life offering a stable coagulation and the antidote. Currently, this is a \$400/400 million market which is not a blockbuster, but can be quoted as a sizeable "nichebuster" nonetheless.

Likewise, we are pursuing a similar tract in oncology where we are targeting typical indications but also factoring the possibilities that come with a stem cell mobilizing molecule. Again, this is short-term requiring less patients in clinical studies which potentially interests more pharmaceutical companies as you are able to enter the market more rapidly while developing other additional clinical indications.

Thirdly, we have an oligosaccharide orally absorbable drug that had never been successfully developed. Therefore we took an innovative delivery formulation and tied it to an out-of-patent anticoagulant medicine on the market in order to develop a new offering in an abbreviated time span.

In using these different approaches we have developed ways to access the market in a relatively shorter period than those starting from scratch. This diversified approach makes a lot of sense for small biotech's looking to compete in a world populated by big pharma. It's not rocket science; it really requires common sense and in my opinion you have to keep it simple.

The French biotechnology industry has been a bit behind its global competitors; what do you feel needs to change?

France is a wonderful country but it unfortunately lacks a couple of things the first of which is entrepreneurs because they're the building blocks of biotech companies. These people are not scared to jump into a bumpy business. Of course, this all starts at university because the entrepreneurial mindset is fostered at this level and France has a classical approach to education.

Secondly, the proper financing infrastructure has to exist. Aside from some public financing, it's difficult to find money in France which clearly needs to change. The public market needs to change as well; the IPO market was difficult before, now you can forget about it! If there you don't have a dynamic market it's difficult for investors to enter and exit.

In my opinion, the market needs to be shaken because it looks fairly sleepy at the moment. However, the long term remains to be seen and the French government appears to be willing to make some moves to stimulate biotechnology.

Endotis' current business model is to develop compounds in-house and license out to market such as with Sigma-Tau most recently. Of course, at this point in time for many biotechs it's essentially a necessary model to access the market. Is this the model of the future for biotechnology companies? Is it worth while to grow out different operations of the business?

There have been many good examples of biotechnology companies doing this such as Amgen, Genentech and Actelion but how many other companies have there been that were unable to grow to this size? One shouldn't be dogmatic in this job rather assess each situation as it comes through the pipeline and see if partnership opportunities exist.

There is no reason you cannot internally market a typical pharmaceutical compound if it is in a niche/specialty clinical indications but it doesn't make sense to start with the decided philosophy of becoming a so called full fledged pharmaceutical company. If you can push a compound further down the trial pipeline then it makes sense to start to think about it as a possible alternative, but not more than that as the value will inevitably be higher at a later phase. However, this is an added risk because should you run into a problem during this phase you are dead in the water. Therefore it makes sense to balance the risk while going after reasonable opportunities and looking for partnerships in areas where you cannot develop internally.

The question after this becomes what to do with companies like Endotis after initial success because it doesn't make sense to go through the same process all over again. In my opinion, you should prove your case, build the value and find the best option out for shareholders and all stakeholders. As a whole, the biotech industry is in transition as it moves from initial round

financing to something altogether new.

Venture capital companies are likely thinking along similar lines at the moment as they appear to finance either early stage companies with unique platforms or later stage companies with compounds close to or with proof of concept in patients. In the middle range where most biotech companies currently exist it's difficult to raise money and draw attention.

How do you move from the grey area in the middle to the late stage companies that investors are looking for?

You have to move compounds from candidates through the pre-clinical stage and up through the Phase cycle until proof of concept in humans. If you cannot move quickly through these stages then you will be in trouble. As I tell people working with me everyday, whether or not you produce value it costs us the same amount of money, but where it matters is in our IP protection. One day lost now is a day of lost peak sales in the future before a patent expires. As I mentioned earlier, timing is of the essence: you have to have a sense of urgency in this industry.

As Endotis moves from a research-driven start-up into a company that brings its products to market, how will you keep this sense of urgency alive?

Our goal is to move as fast as possible to proof of concept in order to partner our compounds with someone capable of bringing them through registration and worldwide marketing. Due to pharmacoeconomics innovation alone is not enough; if you cannot prove that your compound does something better than existing options then you will never get a premium above generics. Today, from very early stage development pharmaceutical companies factor pharmacoeconomics on top of safety and efficacy to ensure they can obtain an acceptable price when they reach the market.

For this reason we have chosen to target such niche market indications where we have a much higher opportunity of bringing something truly innovative to market without competing face to face against big pharma companies. Once you are about to reach or have reached the market successfully you can move from smaller to larger indications. This approach is mimicked by speciality pharmaceutical companies as they look to compete in smaller arenas where they can develop quicker and perhaps negotiate better prices.

With products coming up the pipeline how do you attract your partners like Sigma-Tau?

Our partnership with Sigma-Tau is based on Avidin, our antidote for anti-coagulant which was originally developed by their group for a completely different indication. We proposed that they do their study alongside ours so that they could embrace a wider market in what is a standard 'win-win' situation.

You've had a lot of experience throughout the industry, both in big pharma as well as biotech. What made you return to another French biotech company?

I originally got out to do work on the financial side of the industry (LBO) but the opportunity was soon presented to me to on top return to a directing position in a biotech company concurrently. I was attracted by the people there and we have managed to bring in several brilliant people to build a productive team. Moreover, both therapeutic areas are interesting so the work is engaging.

What motivates you everyday to do what you do here?

Intellectually speaking, nothing matches this industry. I've worked in pharmaceuticals for more than 30 years and I cannot have been bored for more than 15 days during that period. Everyday you come in and there are issues to solve with nice people who are intellectually driven. We truly have to discover solutions to new problems all the time by deconstructing and learning all over again. In this business you cannot take something you have already accomplished years ago and apply it exactly the same because parameters constantly change. If you are ready to use your experience and invent new solutions than you are suited for this job; it's what I like the most about it.

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