Interview with Jen Chen, General Manager, Genovate

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Tags: Genovate

Genovate was founded in 1995. It is a very interesting story: a mix of biotech, the history with American company Genelabs, government investments and also private investment through Chinachem. Can you tell our readers how this company came into existence, what attracted the stakeholders to invest in the company?

After spending nearly 20 years in the States doing new drug development, I am confident that Genovate today has the necessary skills to develop a new drug. When I came back from the US, the most important initial step was to put the right mix of shareholders together. Genovate has three types of shareholders, each is crucial for the successful development of the company. The first of these is the government, as we know that for a pharma company to be successful, regulatory synchronization is the key. You have to work with the government to make sure that regulatory issues can be managed.

I also thought it was necessary to have successful private Taiwanese business involved at a shareholder level. Taiwanese people are particularly business oriented, and have had great successes with high tech products over the years. I wanted to learn how to become a good OEM, and how to turn it into a profitable business. Biotech in a global sense is not a profitable business. Having these business minds on board was key to discovering the best way to run a biotech company that was also profitable whilst it was in its development stage.

The third key shareholder is US biotech. No matter what happens in the Asian biotech sector, people will always look at the US as the golden standard. In Taiwan, 16 of the top 20 companies

are multinationals. This is not because they make generics better than local companies, but because people still have the preference to buy imported generics from well-known brand companies rather than from local companies.

Another key factor in the creation of Genovate is that the founders had a very clear understanding that working on new drug development in a biotech company can be an extremely risky business model if this is your only method of becoming profitable. At the time of the company's creation in 1995, out of about Nasdaq listed 315 US biotech companies, only 3 or 4 were making money. The other 310 were losing money. Today the number of companies stands at around 340, and still no more than 30 are profitable.

This is not well understood in Taiwan, where we are used to seeing industry that very quickly becomes profitable. Out of all of the country's listed companies, around 98% are making profit. As a result of this, the business culture in the country is that all companies work towards their IPO. Making money is not a goal, not a dream – it is a must. The US model does not apply here, because private investors will always expect your company to become profitable very quickly, and this is very difficult to do with a biotech company.

As a result of this situation, Genovate had to very quickly asked itself when it would be possible to break even. If the company was focused purely on new drug development, the first time it would be able to start making profit would be when a Phase III product reaches the market. This means that in order to be successful, it is important to recognise the need to balance this high risk activity with other low-risk and profitable business, to make sure that revenues come into the company at an earlier stage. As a result, in 1995 we started the company, and in 1997 we bought BMS' Taiwanese manufacturing facility. The reason is very simple. We spent $10 million USD buying the BMS plant. Our plan at the time was that in three years, if BMS cancelled all of their OEM contracts with Genovate, we still wanted the facility to be profitable. From day one, we told our plant managers that their job was to quickly increase the number of Genovate's OEM clients. At the same time, in five years, they had to break even and create a self-sustaining business.

We knew we needed a manufacturing site because when the company started its high-risk biotech developments, it was clear that a low risk 'kitchen' would be needed in order to develop and market niche generics plus new formulations for the regional market. We bought the plant, and at the same time told the BMS General Manager that we wanted a piece of the local marketing opportunity. Today, our sales team is about twenty people – still the top four people here are from the sales team for BMS products.

Genovate has OEM manufacturing, sales and marketing, and also clinical trials. We hired Albert Liou to lead our clinical trials team, because when we started the company we brought all the clinical trial compounds from US Genelabs. We quickly set up a 25-person clinical trial team, the biggest in Taiwan at the time. Back then, Merck and Pfizer did not even have clinical trials here – GCP didn't come to Taiwan until 1997. A lot of education was needed to introduce the idea of clinical trials to Taiwan. After a while, Albert became known as the clinical trial expert in Taiwan. I told Albert my priorities: that our trials could fail tomorrow, but that I did not want to lose any staff as a result. I wanted to make sure that after hiring people for Genovate's clinical trial the next priority would be to launch an independent CRO service, so that whether Genovate's trials were successful or not, the company would not lose that section of business. That's how we started the CRO business: we made sure that we had a good balance between our own R&D work and CRO contracts.

In our OEM business, there was a question over conflict of interest between producing our own generic drugs and contract manufacturing originators' drugs. Every company that came to us looking for a manufacturer asked us the same question, Roche, Abbott, Daiichi Sankyo: they all asked why they should give us OEM work when Genovate has its own generic business. This was the same with clinical trials. So we managed to come to an agreement whereby if we contract manufactured for a company, we would not do any new drug work in the areas they had asked us to manufacture. For example, we work for BMS, so we do not make BMS generics. I turned this conflict of interest into mutual win-win: I could either make the generics and risk damaging the company's relationship with its clients, or respect the boundaries. Whenever we make a new generic product, Genovate is always number one or two in the market. This is because after manufacturing originator drugs, the expertise required to manufacture generics comes easily.

What is the revenue mix for Genovate like today?

Without big blockbusters, we can only make small revenues from the generics side. Right now, the company is making around $15 million USD annually. Still, compared to the other local generics companies by reimbursement pricing, we are number 9 or 10. Many local generic companies started from the marketing side. We only have a small marketing group, so the company contracts its sales to distributors. By marketing these drugs ourselves we could increase revenues by two or three times. However, we want to focus our efforts on the R&D side. Our choice is not to boost our local generic business: our choice is to keep on pushing from the new drug side. Hopefully with one new drug, Genovate can be number one in Taiwan, and then the generics business will become a minor concern. Before that happens, I want to make sure that Genovate has its own positive

cashflow. This is why we keep the small but profitable generics/OEM business. The purpose of this is to make sure that our new drug eventually can become successful.

An example of the way in which Genovate approaches new drug development is a patch that we are currently working on. When patients undergo chemotherapy one of the side effects is vomiting and nausea. Today, when you have chemo, you use injectable and oral 5-HT3 blockers to prevent/treat the nausea and vomiting happening in one to five days after chemo. Since the half-life of oral 5-HT3 blockers is very short, and when you are vomiting the overall efficacy of oral 5-HT3 blockers is not very good. We know all of this because the company is involved in clinical trials: we have our own patented anti-cancer, so when we do clinical trials with our own anti-cancer drug, we had to buy these very expensive but not so effective anti-vomiting agents for our patients. From our market intelligence and clinical trials, and talking to oncologists, we realised that we could use a long-acting patch to release through the skin the steady and efficacious amount of the anti-vomiting agent. Right now, the market for 5-HT3 blockers is already worth $1 billion USD, but a satisfactory and patient-friendly patch has never existed in the world, which can give you a steady stream of medication without the up and down problems currently faced by patients. We thought about this, and made a prototype in the lab.

In Taiwan, because of modern technology and market intelligence from the rest of the world, both oncologists and patients are highly educated. That means that when we do market research, it is not only for Taiwan: you can really get a sense of mainstream global tastes. Many of Taiwan's hi-tech manufacturers are OEM manufacturers without experience in the development of brand product through extensive market survey, so it is difficult to get the mainstream product concept, because they deal with clients who already have the overall vision. Biotech is different: because foreign companies always use Taiwan as a market training ground, to test the Asian population response and popularity of their new drugs. When we came up with this patch concept, it came from the accumulated intelligence and that can be further repeated.

After we found that this would be a very lucrative product, we discovered that there are only two competitors. One is a small company from Princeton. The other is a company from the UK called ProStrakan. They have a much larger patch than ours, which is administered once a week. Because we have a clinical group, we asked our nurses to test our patch against a mimic of ProStrakan's patch, named Sancuso. We could easily collect data on sensitivity and irritation because everything is under one roof, and can quickly work on finding a suitable size. We realised that the patch is no good for one week because of the likelihood to develop irritation, but twice weekly is actually the best solution. We have just finished a Phase I study of this new product and the result is even

better than Sancuso’s.

It sounds like your clinical trial work is a huge advantage to your new drug development.

Also market intelligence. Clinical trials are not just for technical GCP trials. You get a wealth of information inflow from your trial. We can turn this good information into new drug design or into market intelligence to understand the mainstream taste of what is going to be the next generation of new drug.

Clinical trials are obviously very important for Taiwan: it’s a very big market – you have more clinical trials here on paper than China. It’s very strange to see. Harmonization has the potential to let Taiwan grow its domestic clinical trials and become a centre of excellence in Asia. What potential do you see in the next few years in those regards?

Taiwan also has more international trials taking place than Japan. Japanese global trials are less than 50. China only has between 10 and 15. Taiwan has over 200, and Singapore about the same. These two countries are leading the market for multinational trials. You may be surprised about Japan. When I say multinational trial it means for global filing. Japan has several hundred trials, but only for the Japanese market.

Nature magazine asked the same question in 1997 during an interview that I gave. I was the first person to tell the government and the international community that Taiwan could be a centre of excellence for clinical trials in Asia. 13 years later, it is still true. Your question is whether we can be that, but I am telling you that 13 years ago, we were already proceeding in that direction.

The evidence that this is already happening is there: Parexel purchased Apex International, a Taiwanese CRO originated from Genovate. Quintiles has a small business in China, but a very big and profitable business in Taiwan. By the way, quite a few Quintiles employees in Taiwan came from Genovate.

We have demonstrated to the world that we can build a very successful clinical trial industry. This has led to multinationals like Merck and Novartis to really consider Taiwan as one of their global centres for clinical studies. Today, the numbers speak for themselves. Today’s job is not to continuously tell people that Taiwan is a centre of excellence. Now the country is being used like a five star hotel. That is not right. Today, we should ask how we could use our facilities to launch our own new drugs. Government money should not be spent on continuing to promote Taiwanese clinical trials to multinationals. They should instead use this very nice infrastructure to cultivate PI initiatives and local trials for global filing. Five years from now, I want to see when ‘centre of

excellence’ becomes a slogan again, with all those Phase II and Phase III trials done by local pharma companies.

What do you think about harmonization between China and Taiwan?

No problem. Harmonization is actually already happening from the foreign pharma companies that have studies here. When people talk about harmonization there are two types of observations. The first is the idea that people want to conduct trials in Taiwan then hope the results can be recognized in China. That is a bad idea. The governments will not chase after those trials. Another direction is that when you design a Phase II/III trial today, you proactively use the same protocol and include sites from China and even Korea. For example, Qualitix, Genovate’s CRO business, is today doing quite a few trials to include countries like Singapore, Hong Kong, Taiwan, Korea and China together. When you proactively harmonize trials, ICH will not be a problem and a good platform to seek regional regulatory recognition of such mutinational studies.

You were saying you need to cultivate local trials, and what is needed is for Taiwan to host its own trials.

Right now, Taiwan PI’s are seldom the first author on clinical trial papers, because we are not leading the way. When local companies only produce generics, it is natural that Taiwan’s most respected researchers and professors only work for the big multinationals. However, they are waiting for Taiwan to develop its own innovative products, and will happily work to boost the national industry if there is the opportunity to work together. We see that trend coming.

For example, Sanofi Aventis launched an anti-obesity product called Acomplia in 2007. They launched it for almost a year, then withdrew it because it approximately doubled the risk of developing psychiatric disorders than those taking a placebo. They made about $112 million USD, then suspended Acomplia sales in the Europe. The US FDA never approved this drug. It was not only an appetite suppressant, eventually it became a mood suppressant and led the patient to develop suicidal tendencies. We initiated an Acomplia ‘me better’ programme in Taiwan in collaboration with NHRI (Taiwan NIH). We have the skills to very easily complete a quick follow up programme. But then, when this withdrawn came along, we were faced with two choices. One was to withdraw like the other twenty pharma companies who were working on a ‘me too’ drug. Here at Genovate, we made a different choice. We asked how we could turn this to our advantage. We worked to develop a better version of the drug that doesn’t go into the bran, then it will not have the same side effects as Acomplia did, and I am pleased to tell you that today this drug is being very successfully developed. This is a business model that I would like to see being repeated across

Taiwan, as it allows companies here to exercise their main strengths, and take advantage of the opportunities available for developing innovative products.

Looking at your business model, it looks like the way that Genovate has developed is that it sees a way to expand and then vertically integrates this into the business, and it brings Genovate added value. We talked before the interview about the profitability of APIs for example. In the future, is that something that you would consider? How are you going to grow the business in the years to come?

The API business in Taiwan is already a proven success for those companies that started off with a focus on generics because just like US companies, when you have a generics business, you always have your own API. If you don't, you lose control of your quick generic launch potential. This was the reason that IVAX eventually got purchased by Teva, for example. The top three Taiwanese generics producers (YSP, Standard and CCPC) all have their own API business. They are also all listed. They are all profitable. Sometimes their profitability is even better than their generics. The API business in Taiwan is very seasoned. Siegfried is a very large Swiss API business. Even as far back in the 1980s, they came to Taiwan having recognised the country's potential and started their API business here. This became the first local API joint venture. Today, they make a very profitable business.

However, Genovate does not want to enter the API business. I want to eventually have a business like Kos or Shire, specialty pharma companies. Kos was acquired by Abbott for $3.9 billion USD after developing a product called Niaspan (an extended-release tablet of nicotinic acid). This drug today has a market of around $800 million USD. Kos only spent $40 million USD to make that controlled release product into a blockbuster. This is the key: selecting the right product and then waiting for big pharma to come and purchase your company and become the leading brand through that company. I believe Taiwan's 'me better' strategy will allow us to do this. Before that success however, you need to find a different way to support your work. API certainly is not Genovate's strategy. Ours is to use our OEM and CRO, and also generic business to balance the risks of new drug development.

What do you want to tell our readers as a final message about Genovate?

We hope that in five years from now we can be the regional leader in specialty pharma. Today, we have products in Phase I and pre-clinical. Hopefully in five years, these drugs can be licensed out to big pharma. This means that we have to prove ourselves as a competent new drug developer, not a generic company. All of Taiwan's companies today share the same dream. However, we are building our dream, but through a very practical and solid method.

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