Kai Lamottke – Co-Founder, Managing Director (Germany) & General Manager (China), Bicoll



Half of the top 200 drugs in the world are inspired by plants

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Dr Kai Lamottke, co-founder and MD of Bicoll GmbH, Munich, and since 2001, GM and board member of Bicoll Biotechnology (Shanghai) Co. Ltd discusses Bicoll's presence in both the Chinese and European markets, its unique Bicoll Plant ProfilesTM (fine fractions derived from plant extracts fractionated by Bicoll's innovative isolation system Bifrac N), and the company's strategy to capitalize on China's innovative life sciences market.

Kai, after studying in both Germany and the United States and setting up Bicoll in Germany, why did you decide to come to China?

While studying at the University of California Berkeley, I came into contact with several Chinese students and in particular a student from Taiwan who I learned a great deal from. Furthermore, in 1994, I visited China and was impressed by the Chinese culture. As I returned to Germany for my PhD, I met a Chinese postdoc with whom I debated both the ongoing crisis of ideas for pharmaceutical invention as well as for research and development (R&D). At the time, many approaches, including combinatorial chemistry, calculations (what has to be done to increase productivity), and what needs to be increased in terms of numbers, were discussed. However, "Quality" aspects of used starting points as drug discovery compounds was an overlooked issue in this kind of "number's game" from our point of view. According to our analysis, the source with the

highest “quality” of ideas as a starting point for drug discoveries are compounded from plants.

Half of the top 200 drugs in the world are inspired by plants. In general, (big) pharmaceutical companies do not have a ready to go answer to create fast new qualitative high starting points for their research. When they create compounds, it comes down to the quantity. Generally, it can be difficult to get fast answers if the used models simulating your hypothesis of a (human) disease are not exactly fitting. It has to be accurate and you need to be assured that the biochemical assays, biological assays, and the animal models are in line and correct, in place, and delivering robust read-outs. We have analyzed the speed at which we can quickly deliver a series of relevant compounds to be able to get consistent answers among these assays. For example, as a case study, we took a development cycle from one of our partners in the food industry: from the initial source to having a product ready for the market in one year. If you were to present this timescale to the pharmaceutical industry, they would be shocked and very skeptical, as there are many arguments as to why this may not possible in the pharmaceutical industry. However, there is no faster method available on the market than what Bicoll has done in getting fast answers from initial screening to first animal data, of which it has been disclosed in peer-reviewed papers.

Our collaborators are getting a rapid indication as to whether their hypotheses are geared towards developing new drugs, and if their intended compounds have a high chance to deliver positive results in clinical trials, of which they can then proceed to use these drugs in the future. Historically, Bicoll has used these plant-based natural products for quality reasons. Furthermore, we began to offer medicinal chemistry competence to allow us to produce solid patent protection, which enables us to figure out the most relevant modifications for human patients.

How is Bicoll split and run in both Germany and China?

Most of our lab work is done in Shanghai. In total, we have 30 people divided between two locations. We see ourselves as contributing input on a level of cutting edge science. Some of our partners accept us being a part of their patents as well as part of their publications. For example, we were involved in a publication of deorphanizing orphan targets together with a French company. As a company, we are trying to quickly find an answer to the question: can we see positive effects within an organism if you bind a ligand to a previously unknown target or enzyme? Mostly, new biotech companies do not have a single compound available despite conducting several years of research. This is caused by the lack of resources to synthesize enough chemical starting points to progress on their research path. However, in the nine months after Bicoll’s

involvement, we were able to deliver 30 different starting points in four different kinds of compound classes in the mentioned case above.

Our industry hardly understands its own success models. Thinking about the long development cycles in this industry, which can last 12 years for example, where the CEOs are often subject to change every three years. This means that a CEO currently in place will lay the groundwork of the CEO four or even five cycles on. This happens if you are thinking about managing R&D correctly. In big organizations, there is easily a disconnection between what is being done today and who will profit from this in the future. Due to having such long cycles, from a management point of view, it is always good if the person who solves the problem also profits from it. This may be why biotechnology companies with their concept of ownership-driven hi-tech science approaches might be seen as more innovative and successful by aggressively using their resources.

You have the technical platforms, Bifrac NTM, Bicoll Plant ProfilesTM, Bilobac NTM, and BIPRESELECTTM. Can you tell us how your clients and partners benefit from these platforms?

As we started the company, it was a challenge to compete with any synthetic approach due to costs per compound. When it comes to chemistry, the costs of high-throughput screening are in the millions. Furthermore, it was a problem of having the same amount of numbers provided to partners for screening. This is the first interaction and interface for us and our partners. We are sorting the physiochemical properties of the compounds found in our starting materials. It shrinks any interference in the detection and produces very robust readouts with pharmaceutical like compounds, which have proven their success already in influencing human metabolism. Flipping this around, because plant ingredients are the most successful sources of new pharmaceuticals, if they do not fit into any screening system, then you will not be able to identify the drugs of the future.

There are many other projects underway. For example, we are also collaborating with the Charité in Berlin, which is one of the largest university hospitals in Europe and a medicinal-based research hotspot.

A recent press release has announced there were promising anti-seizure results with your own small molecule lead structure. How will this product change the lives of

epilepsy patients?

We are still in early research. It is based on a hypothesis with our work on a derivative of other natural compounds found in plants. Our starting point was from this type of derivative, where we are trying to understand if this compound has the chance to influence brain metabolism. At the start of the project, 16 legal entities were running over five years with EUR 12 million (USD ~13 million) in funding. At the time, we were facing a lot of interesting hurdles in the drug development and drug discovery approach, because it is tough to picture an epileptic event at the protein level or in model organism correctly.

In Europe, it was a little difficult to receive the approval for animal testing. We needed over three years for the initial toxicity and biological screenings. In the end, we found a solution. We decided to test our compound on leftover human brain tissue from surgeries conducted on epileptic patients. These brain tissues can be kept alive for some time, and they were sufficient for us to generate data that eventually persuaded the regulatory authorities in Europe to let us progress onto animal tests, where the compound also demonstrated anti-seizure effects.

What is your collaboration strategy?

Life is a collaboration and success depends on how to manage different kinds of collaboration, where both parties should profit from it. Within the industry, companies understand that the majority of innovation will take place outside their walls. The question from their point of view is, how can they be sure that the ecosystem around their companies is productive and conducive for different kinds of collaboration?

I have seen how the San Francisco Bay area has evolved over the last decades and I have also seen how one of the top local European biotech clusters in Munich has evolved, too. In addition to this, I have watched the biotech scene progressing in Shanghai for over the past 20 years. That requires a long-term commitment from everyone involved. This includes employees, infrastructure and government.

Currently, we have Chinese clients with a slightly different kind of perspective to research. What you can contribute and what you should contribute looks rather short term and opportunistic, meaning currently we do not approach others in China systematically and ask them for collaboration. However, I am optimistic that this will change soon. Most businesses come to us for help and support, they have heard about Bicoll’s capabilities and have read about our

achievements.

In China, employees tend to hop between positions at a faster rate than in Western countries. How do you handle both talent acquisition and longevity?

First of all, you have to work on creating a functional team, which takes time. There is also a need to involve new people. I try to point out that we are research-driven as well as interactive, which is how we do business. The way we do business seems to be unique in China and may not be understood by everybody coming into our company at first. Yet, others may enjoy the differences in how we operate as they understand that you cannot easily find this environment elsewhere. Secondly, it is difficult everywhere to acquire talent but around 75 percent of our employees have stayed at Bicoll for more than ten years. So, from this perspective, we are glad to have such a good retention rate.

It can be difficult to form collaborations in countries such as China due to language barriers and cultural differences. How does Bicoll maintain close relationships with the Chinese industry stakeholders and do you mainly have multinational or local collaborations?

I can see China is very open to international interaction, but people are normally more comfortable speaking their own language. Employees at Bicoll who are native Chinese speakers represent Bicoll in the local communities. We have many collaborations, but we primarily work with European-based research institutes as well as companies, both multinational and local. From a public perspective, we are more visible in Europe than in Shanghai for many reasons. However, we try our best to invest in this kind of visibility, but it can be tough for smaller organizations if they do not have the professional support, primarily because interacting with the media is only taught to a certain degree in natural science education. And most of the colleagues at Bicoll have scientific-educational degrees.

What is your current client portfolio?

We are looking at whether the counterpart is open-minded, research-driven, goal-orientated and fits our approach of working on relevant questions such that humans can benefit. It is less about

the company structure, rather the interaction between the people inside the company. We then establish an understanding of how to interact, deliver, and provide efficiency to the benefit of our partners. If organizations succeeded in reaching out to us, this means that they are successful in their market, as interacting with us is an indication that they can leverage outside knowledge and to bring outside knowledge into their own companies. Companies that are very restricted in what they do, and their assessment, are lacking behind in their overall performance on the market, as such they will also have a hard time finding us.

Moving forward, what are Bicoll’s main priorities?

To get the right people around the table, either inside the company or outside the company as collaboration partners to expand our knowledge about the next generation products which we are all interested in working on.

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