Nicolas Fischer – CEO, Light Chain Bioscience

There is no question that bispecific and multispecific antibodies represent novel modalities that enable unique modes of action and possibilities for therapeutic intervention

16.03.2021

Tags: Switzerland, Biotech, Light Chain Bioscience, Strategy, European Biotech

Dr Nicolas Fischer introduces Light Chain Bioscience, a Swiss biotech company focusing on the discovery and development of bispecific antibodies using proprietary technology. Fischer also outlines the competitiveness of Light Chain's platform, the company's partnership strategy, and his goals for future growth.

Nicolas, could you start by introducing yourself and briefly the story of Light Chain Bioscience and how it is related to the Swiss biotech company Novimmune?

I completed my PhD in molecular biology at the University of Geneva and then took a postdoctoral position at the Medical Research Council in Cambridge in the UK. I joined the laboratory of Sir Greg Winter, who, incidentally, won the 2018 Nobel Prize in Chemistry for his pioneering work antibody humanization, phage display technology and its application to the development of therapeutic antibodies. This was when I entered the antibody engineering space, moving away from pure academia into more industry-related areas. I was also exposed to the dynamic biotech environment in Cambridge, and during that time a new antibody company had been created, generating quite some excitement in the Winter lab. This was really an eye opener and pushed me into the world of biotechnology.

Following that, I had the opportunity to join Novimmune in 2002, then a small start-up that had been founded by Professor Bernard Mach at the University of Geneva. Progressively, we started

developing our portfolio, with a focus on immunology and inflammation and the identification of human therapeutic monoclonal antibodies (mAbs).

Initially, Novimmune did not have any proprietary technology, but we were licensing in technology platforms from other companies to support our discovery activities. Eventually, we took six mAbs from discovery into Phase I clinical trials. One of those, now known as emapalumab, advanced much further than we initially anticipated, all the way through to Phase III and then regulatory approval by the FDA. It has been a fantastic achievement for a small company such as Novimmune and we all learned a lot along that journey. We needed a commercial partner to bring this drug to patients, and we partnered with the Swedish rare disease player, Sobi. Initially as an exclusive licensing agreement in 2018, but a year later, in 2019, Sobi decided to acquire the molecule as well as related assets, which included the core team that had worked on emapalumab – about 110 people out of the 160 employees working at Novimmune at the time. The remaining group was going to focus on the discovery and development of bispecific antibodies using our novel proprietary technology. After the divestment of emapalumab, we rebranded as Light Chain Bioscience.

What is the intended focus of Light Chain Bioscience and how is it different from what Novimmune used to be?

Light Chain Bioscience focuses on the identification and development of bispecific and multispecific antibodies using our proprietary format called Kappa-Lambda body™. As I mentioned, at Novimmune we used in-licensed platforms to support our internal mAb discovery programs. These platforms included transgenic mice, as well as human antibody phage display libraries and we also occasionally performed antibody humanization. With these three core technologies, which all come with their own pros and cons, we acquired a solid expertise in antibody discovery and engineering. Progressively we also started to develop our own antibody generation technologies, not only to increase our independence and freedom to operate but also to enable the development of next generation antibody formats. Of course, other benefits of having an in-house platform, are higher flexibility and faster turnaround times.

There is no question that bispecific and multispecific antibodies represent novel modalities that enable unique modes of action and possibilities for therapeutic intervention. Even if immuno-oncology is the main focus of attention the range of applications has been expanding tremendously, including inflammation, neurodegenerative and infectious diseases as well as

hemophilia, an area on which we had a collaboration with Shire and Takeda using our platform.

Importantly, many of these novel modes of actions cannot be mediated by standard mAbs or combinations of mAbs. On another hand, we also were absolutely convinced that the success of mAbs was in part due to the fact that they are very well-tolerated, having low intrinsic toxicity. In contrast, bispecific and multispecific antibodies are inherently ‘unnatural’ as two distinct specificities must be combined into a single antibody molecule. When we started working on the development of our platform, the existing bispecific technologies typically involved different protein engineering approaches to combine two or more specificities within the same antibody. This was mainly achieved through the introduction of mutations, linkers or other protein modifications.

With these elements in mind, our goal was to develop a multispecific format maintaining the natural structure of a human antibody to generate drug candidates that will have a higher likelihood of success in the clinic. We achieved this goal with our Kappa-Lambda body™ platform, that delivers bispecific antibodies fully retaining the natural sequence and structure of human antibodies, without a single modification. To build and isolate these unique molecules, we rely on the use and properties of antibody light chains. To reflect this new focus, we chose the name Light Chain Bioscience.

Many companies – Big Pharma and biotech alike – are developing their own antibody discovery platforms to grow their pipelines. How competitive is your platform?

Most pharma companies with a focus on biologics have either developed or access some sort of bispecific antibody platform. Over the last decade there has been an explosion of approaches to address the challenge of effectively generating a bispecific antibody. As a result, today, there are over a hundred ways to make a bispecific antibody. Of course, creating such a molecule in the laboratory is just the first step on the journey leading to the commercialization of a drug. The next hurdle is to be able to manufacture the antibody, it needs to be stable in an administrable formulation. An emerging concern with bispecific antibodies, is immunogenicity (the ability of a foreign substance to provoke an immune response). This might in fact not be very surprising, since even completely natural human proteins or non-engineered antibodies can elicit an immune response, as such the more artificial the molecule, the higher the likelihood for running into such problems. We believe we have an edge with our platform, since we are creating bispecific antibodies that are as unmodified, retaining the drug-like properties of a mAb. As more and more

are bispecific antibodies based different formats are now being injected into patients, we will gain more insights into these aspects in the near future as drug candidates progress through clinical development phases.

Most within the industry would probably agree that combining multiple drugs is needed to treat severe diseases and combination therapies have become standard in oncology. Not surprisingly, the appetite for multispecific modalities is clearly there and is increasing. However, there is a tendency to think that one can simply combine two mAbs together in a bispecific antibody format to create a good bispecific antibody candidate. Personally, I think this an over-simplification because bispecific antibodies often require a particular geometry to enable optimal biological activity. If you want to make a bispecifc antibody, there needs to be a strong rationale behind the need of incorporating each of the specificities into a single molecule rather than considering a combination of two mAbs.

Now that you have your own technology platform, you are both working with partners that want to use your platform as well as developing your own pipeline. How are your energies and efforts split between both priorities?

Indeed, we have a hybrid model. Around 60 percent of our capacity is dedicated to our partnerships. We have pursued a number partnerships for the generation of Kappa-Lambda body™ with pharma and biotech players, including Takeda, LamKap Bio, and the discoveric bio Group. These companies come to us with their own ideas or concepts for novel bispecific antibodies, in disease areas that fall under their expertise. We work with them to bring the therapeutic molecules they are looking for from concept to identification of a drug candidate and into preclinical and early clinical development depending on the requirements and internal capacity of our partners.

Our current internal focus is immuno-oncology, and we dedicate the remaining of our capacity to drive and advance our proprietary projects. This gives us a nice balance of revenue generating partnerships and internal programs driving innovation and value creation.

In terms of your own pipeline, what is your strategy and what are your current flagship programs?

As I mentioned, we focus on the development of multi-specific antibodies, especially bispecifics in immuno-oncology. One of our main angles of interest is the immune checkpoint CD47, which is an

extremely hot target at the moment. Our flagship program NI-1701/TG-1801 is a CD47/CD19 bispecific, which we are developing in partnership with TG Therapeutics who is driving the Phase I and II trials. Following the same concept, we also have another Kappa-Lambda body™ targeting CD47 and mesothelin for solid tumors for which we are filing a clinical trial application. We expect this asset to enter clinic trials before the end of this year. In addition, we are combining our CD47 approach on other targets for the treatment of solid tumors. Beyond CD47, we have programs exploiting T cell retargeting and other modes of action that are relevant in immuno-oncology.

We are regularly having partnering meetings with Big Pharma players to discuss their potential interest in our programs as our objective is not necessarily to take our assets into Phase II or III trials. Now, if we have a very successful Phase I molecules, we might advance further but so far, we want to focus on what we know we are good at, discovery and early development.

We also have a number of proprietary mAbs for which we have been actively looking partners. For instance, we partnered with Canadian player Edesa Biotech last year to explore the use of one of our anti-TLR4 mAs to fight the inflammation associated with COVID-19. Finding partners for our mAb portfolio also allows us to focus on our bispecific and multispecific assets, which we see as the future of the company.

For a biotech company, your financing situation is a little atypical and unique. How does this change how the company operates?

We are a private company and, as I highlighted, we have a regular income stream through our technology platform and discovery partnerships. We are also supported by investors and are very fortunate in terms of our financial situation. This allows us to effectively advance internal programs and reach our mid-term goals. We also just moved into brand new facilities that we designed so that they are optimally suited to support our activities.

We revisit regularly on our partnership models so that we can continue to operate under this hybrid model combining partnerships and internal pipeline. We are flexible in terms of how we partner with companies, including large and small players, and rather than being technology providers, we work with our clients more as partners to achieve their goals. Having our own internal pipeline also helps in the sense our assets further validate our technology platform. When we discuss with potential partners and describe our assets and unique bispecific approach to target CD47 they can be interest by the asset itself but also by deploying our technology and approach on another oncology targets that are of interest to them.

Speaking of platform technologies and oncology, the US is obviously the largest oncology market globally, but China is one of the next in line. Is Light Chain Bioscience at the stage to be thinking about the Chinese market?

Certainly, the Chinese healthcare market has grown tremendously. We are already in contact with a number of companies in China but we have not struck any partnership yet, though we are completely open to it. A number of Chinese companies also do reach out to us regarding our technology platform or Chinese rights for some of our assets. What also is increasingly attractive to us as a company is the opportunity to accelerate the progression of our pipeline by potentially conducting clinical trials in China but we would approach that in partnership with a local player.

How do you evaluate the Swiss biopharma innovation ecosystem? Is Switzerland doing well in terms of translational research, talent attraction, financing and so on?

Switzerland has clear strengths and is an environment promoting innovation which is fueled by many great universities, top engineering schools and research centers. There are a lot of talents in the country, and foreign talents are also happy to move here, so there is no shortage in this respect. Over the past 20 years, the ecosystem has become more supportive, with the creation of incubators and accelerators, laboratory space has also become more available. I do like the fact that there are many small biotech companies in Switzerland and of course, we have our national champions. However, when compared to global hubs like in Boston in the US or Cambridge in the UK, we can certainly do better. Risk-taking attitude and enthusiasm can be developed further, no question about that.

Looking forward, where do you expect to see Light Chain Bioscience in the next few years?

Our bispecific Kappa-Lambda body™ platform has now reached a high degree of maturity and validation in terms of discovery and developability to reach the clinic. Based on this solid foundation we will pursue our parallel strategy of working with partners as well as progressing and expanding our internal pipeline. In doing so I expect that in a few years we will see a number of truly native bispecific antibodies based on our unique format under clinical evaluation. Another important mid-term vision shared by the leadership team and supported by our investors is the

development of our multi-specific approach enabling even more complex modalities, while keeping a fully native structure

See more interviews