Chris Martin â?? CEO, Co-Founder and Director, ADC Therapeutics

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Dr Chris Martin, CEO and co-founder of Swiss-headquartered antibody-drug conjugate cancer company, ADC Therapeutics, shares the companyâ??s journey over the past decade, the exciting progress of their two lead candidates, the process of building their commercial organization in the US, and his perspectives on Big Pharma partnerships.

Chris, could you quickly introduce yourself as well as your journey with ADC Therapeutics?

I originally trained as a chemical engineer, obtaining a DPhil in engineering science at the University of Oxford and an MBA at the Institute for Management Development (IMD) in Switzerland. After that, I became a serial entrepreneur, co-founding a number of businesses â?? outside of biotech initially â?? but I eventually moved into biotech around the early-2000s, where I started to look for interesting therapeutic technologies in which to invest. I was particularly focused on oncology so I looked at a lot of oncology technologies, and I eventually came across pyrrolobenzodiazepines (PBDs), a technology coming out of University College London (UCL). PBDs had been rationally designed by the professors there to be active in patients with tumors that had become resistant or were originally resistant to a lot of therapeutics.

I thought this was very attractive and made a small investment to form a company around the technology. This became Spirogen. Around 2010, we realized that PBDs were very attractive as

toxins for antibody-drug conjugates (ADCs), and based on that, we worked on a number of partnering deals with companies like Genentech, Seattle Genetics and AstraZeneca.

In 2011, we spun ADC Therapeutics out from Spirogen to focus on developing a pipeline of ADCs. I stayed on at Spirogen and, when we sold Spirogen to AstraZeneca in 2013, I became a member of MedImmuneâ??s Management Leadership Team and AstraZenecaâ??s Senior Leaders Group. Eighteen months later, I left AstraZeneca to assume the CEO position at ADC Therapeutics. I have been with ADCT ever since.

From your experience with Spirogen and now ADC Therapeutics, what is your perspective on biotech partnerships with Big Pharma? Many biotechs are wary of forming collaborations with Big Pharma players because they are worried that their own assets might not be prioritized or that they will lose control over their strategy.

My experience with partnerships has broadly been positive. They have a role to play, and if managed well, they can bring a lot of value to both sides.

Spirogen was a platform company so we worked predominantly through partnerships. We had very long and very successful partnerships with a range of pharma multinationals. I think successful partnerships rely upon good management and good scientific direction on both sides.

At ADC Therapeutics, we currently have two lead programs. Our plan has been to reach clinical proof-of-concept (POC) and bring these two programs to market in the US ourselves. But we also have a deep pipeline, a very productive R&D team, and great ADC platform technologies, so we are also interested in partnering with other companies for some of these earlier programs. The potential of these pipeline assets to combine effectively with other marketed and novel therapies means that we would like to collaborate on some of our earlier programs, which are equally promising and exciting.

As is clear from the name of the company, ADC Therapeutics focuses on this antibody-drug conjugate (ADC) technology platform. Can you share a little regarding the significance of this technology platform within the area of cancer?

In a way, ADCs are a simple concept. There is the antibody, which binds to a protein that is exclusively or predominantly expressed on the surface of tumor cells. To analogize, it acts as a guided missile. It finds and binds to the tumor cell, where it becomes internalized, and then the enzymes in the cell release the toxin into the cell, so that it can kill the tumor cell. The PBDs, as I highlighted, are very potent toxins designed specifically to be active in tumor cells that are resistant or refractory to many other therapeutic modalities.

The tricky part about ADCs is that they are relatively complicated to develop and manufacture because they combine very potent drugs with complex biologics and antibodies. The ADC platform itself is important but the way the platform develops drugs through to clinical POC is also important. We have a very strong R&D team at ADC Therapeutics that has been able to file â?? on average â?? two INDs per year since 2012.

You currently have two lead assets: Lonca and Cami. Can you tell us your expectations for them?

For Loncastuximab Tesirine (Lonca), we filed our Biologics License Application (BLA) with the US FDA for diffuse large B-cell lymphoma with a target action date of 21st May, so if everything goes according to plan, we expect to launch Lonca in the US mid-2021. We already have our medical affairs team and our salesforce in place, and our medical affairs team is already engaging in appropriate interactions with healthcare professionals.

Lonca is being developed as a third-line therapy for diffuse large B-cell lymphoma. We have presented data at the American Society of Hematology (ASH) Annual Meeting demonstrating good overall and complete response rates across a broad patient group, including patients that are candidates for bone marrow transplants, patients that are not candidates for bone marrow transplants, and patients that have failed or not responded to prior lines of therapy.

The initial feedback from the physicians we have spoken to â?? both in the community and within academic centers â?? has been really positive. They appreciate the profile of Lonca in the third-line-plus setting, particularly its broad activity as a single agent. By the time patients have to access third-line therapies, they have been exposed to many powerful chemotherapeutic agents, so a single agent with a manageable profile and a fairly quick response â?? like Lonca â?? is very attractive to physicians. The median response time is 41 days, and patients with a complete response often see a very durable response as well, with the median duration being over a year. That is very attractive for patients with this aggressive cancer type.

Camidanlumab Tesirine (Cami) is composed of a monoclonal antibody that binds to CD25 and we are developing it for relapsed or refractory Hodgkin lymphoma. We are also developing it for the treatment of solid tumors through a novel immuno-oncology approach where we are targeting regulatory T-cells. In Hodgkin disease, we have just recruited 100 patients for a pivotal Phase 2 study. In our interim results, we saw in seventh-line patients a median response rate of 83 percent and a median complete response rate of 38 percent. It is a very active drug, and we hope to move that forward along the regulatory pathway in the US.

ADC Therapeutics completed its IPO in 2020, raising USD 268 million. What did that mean for the company?

We are very pleased with the IPO and funds raised since then, and I am happy that we brought some very strong investors into the company. The proceeds will go to clinical development of our lead programs, as well as our earlier clinical assets, and also to the development of our commercial organization in the US and the launch of Lonca in the US.

ADC Therapeutics also recently established a joint venture company with a Chinese biopharma company, Overland Pharmaceuticals, to commercialize a number of your assets in Greater China and Singapore. What was the motivation behind this approach?

Overland is backed by Hillhouse Capital, a well-known biopharma investor in the US and China. We are partnering with them with a goal to bring four ADC assets to Greater China and Singapore.

The Chinese market is substantial and the oncology market â?? particularly targeted therapies â?? is growing quickly. There are also more patients with diffuse large B-cell lymphoma in China than in

the US, so it is an important market to us. The JV will participate in our global clinical studies so we will now be able to include Chinese patients in our global clinical development programs. We are very excited to be moving forward with this initiative, and we also hope to IPO the JV company on the Hong Kong Stock Exchange in the future when the time is right.

How have you been recruiting for your US commercial expansion?

In general, we have built the company by recruiting experienced heads of functions, who were then responsible for assembling their own functional teams. The first person to join us when we spun out ADC Therapeutics was Dr. Patrick van Berkel, who came to us from Genmab. He is a very experienced drug developer and protein chemist who built our R&D team, which is based in London. We placed the team next to Spirogen in London so we were able to benefit from the knowledge base there through a collaboration.

We recognized that the US market was really the largest launch market for ADC drugs in oncology, and it was critical to include US clinical centers in clinical development, though we of course do a lot of clinical development within Europe as well. We were also interested in accessing the talent market within the US.

Our US clinical development team is based in New Jersey and is headed by our Chief Medical Officer and head of oncology clinical development, Dr. Jay Feingold, who worked on the first ADC drug ever developed and approved. He then assembled his own team that brought a wealth of ADC development experience to ADC Therapeutics. We also recruited our Chief Commercial Officer, Jennifer Herron, over a year ago and our head of medical affairs Dr. Joseph Camardo around the same time. At the IPO, we also recruited a new CFO, Jennifer Creel, who came to us from Celgene. All of them have done an excellent job of growing our commercial and operational organization.

We are confident that our salesforce can reach over 90 percent of prescribers in the US. We have a really agile marketing and medical affairs team, and we have invested significantly in building our US presence in the past 12 months. We pride ourselves on working in a very flat, flexible organization. We are still a small company so we can make decisions quickly. We work in a very cross-functional manner around each of our assets.

Coming now to ADC Therapeuticsâ?? HQ, which is based in Switzerland, what is the role of Switzerland within the companyâ??s growing global presence?

Switzerland is an incredible place to have a biopharma company. You have some of the worldâ??s leading industry players here, including Roche, Novartis and Lonza. It is a small country but people are very highly educated, the infrastructure is excellent, there are very good logistics and there is a strong culture of supporting innovation. I think the Federation understand the value of bringing high-tech businesses, including biotech businesses, to the country, and they try to help companies become efficient.

It is also an attractive place to recruit talent to, whether from across Europe or even from the US.

Our global HQ is here and we have set up our ex-US clinical development and commercial teams here. We have corporate development, legal, finance and other functions here as well.

The oncology space has become very competitive over the past few years, and many new technology platforms and modalities are emerging. How do you see the future of oncology companies?

At the end of the day, it comes back to patients â?? and unfortunately, broadly speaking, around 50 percent of us will suffer from cancer at some point. In other areas like cardiovascular disease, we have seen a lot of progress in the reduction of mortality rates, as much due to drug advances as to lifestyle changes, but cancer remains a major disease. Technology has advanced sufficiently that we can now talk about cancer as a chronic disease but until we advance much further in obtaining more curative outcomes in cancer, I think oncology will remain a very important area for the industry. We have made considerable progress in many types of cancer but there is still a very long way to go.

It is exciting to see the diversity of therapies that has been developed. From cancer diagnostics providing a better understanding of the genetics of the patient as well as the tumor microenvironment, to the different therapeutic modalities available, from targeted therapies to radiotherapies, the industry is bringing everything together to provide the best possible patient journey. That is the journey that we are on and I think the entire industry is working hard to deliver this to patients with cancer.

A final message on behalf of ADC Therapeutics?

ADCs are becoming a significant therapeutic modality as a targeted therapy in oncology. ADC Therapeutics has one of the most productive R&D and clinical development teams and technology platforms within the industry. We are excited about both our lead programs, as well as our earlier-stage programs, some of which we hope to develop through partnerships. We are guided by one principle: to get effective cancer drugs to the patients who will benefit from them as quickly as possible and to do so for as many patients as possible.

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